NDT Perspectives

European Renal Best Practice (ERBP) Guideline development methodology: towards the best possible guidelines

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ABSTRACT

The prime mission of European Renal Best Practice (ERBP) is to improve the outcome of patients with kidney disease in a sustainable way through enhancing the availability of the knowledge on the management of these patients in a format that stimulates its use in clinical practice in Europe. A key activity is to produce clinical practice guidelines to help clinicians make the healthcare decisions they face. To further improve the quality and validity of its clinical practice guidelines, ERBP has revised its guideline development process. The present document outlines the principles of ERBP’s 10-step approach. Important features include standard procedures for selecting topics, for assembling the guideline development group, for choosing and formulating questions, for finding, appraising and summarizing the evidence, for generating recommendations, for preparing reports and organizing peer review. ERBP has adopted the Grading of Recommendations Assessment, Development and Evaluation system for rating the quality of the evidence and strength of recommendations and has addressed implementation in the development process by integrating the GuideLine Implementability Appraisal tool. Ultimately, it is anticipated that these changes will not only further improve the quality of the guideline development process, but also enhance the quality of care and improve outcomes of patients with kidney disease across Europe.

Keywords: evidence-based medicine, kidney diseases, practice guidelines as topic

INTRODUCTION

The past five decades have brought an unprecedented growth in knowledge. It has resulted in better treatments and better outcomes, but the amount of information has become impossible for the individual to digest [1]. In addition, factors aside from scientific evidence, such as age, comorbidity, patient preference and perhaps also cost influence the healthcare decisions we face [2, 3].

Guidelines are designed to aid medical decision-making with the aim of improving care. Although, if rigorously developed, guidelines can do exactly that, many have questioned the processes supporting guideline development and criticized resulting guidelines for being contradictory, a duplication of effort, unduly influenced by industry, impractical or simply...
not evidence based [4, 5]. A systematic review of guidelines for living kidney donors for example illustrates how different organizations provide different thresholds for blood pressure and weight in setting contra-indications for donation [6]. Most included guidelines also seemed to lack methodological rigour.

In an effort to counteract the—at times justified—criticisms, the European Renal Association—European Dialysis and Transplantation Association (ERA-EDTA) has revised its approach to guideline development. With the intent to use more rigorous methods, and at the same time a desire to provide guidance even when published evidence is absent, ERA-EDTA has agreed that above all, the process should be transparent. This resulted in a change of name to European Renal Best Practice (ERBP) and a declaration of intent in 2009 [7, 8].

Four years on, ERBP has made tangible steps towards using more rigorous and transparent methods for developing their guidelines. It has laid out some general principles based on the standards of the Institute of Medicine [2], those proposed by Guidelines International Network [9] and the quality assessment tool issued by the Appraisal of Guidelines for Research and Evaluation Collaboration [10]. This paper aims to describe ERBP’s methods for guideline development, of which the guideline on kidney donor and recipient evaluation and peri-operative care will be the first practical application (Figure 1). ERBP has developed other formats for providing guidance too. Position statements, such as the most recent on Kidney Disease Improving Global Outcomes (KDIGO) Clinical Practice Guidelines on Acute Kidney Injury, are developed according to different rules, and will not be covered here, but can be found online at www.european-renal-bestpractice.org [11]. Specific issues related to dealing with rare diseases are beyond the scope of this paper and are discussed in another paper in this series [12].

**FIGURE 1:** ERBP guideline development process.

6-month research programme with the Cochrane Renal Group and Kidney Health Australia—Caring for Australasians with Renal Impairment (KHA-CARI). In addition, the team includes a medical informatician with expertise in guideline implementation.

**HOW ARE TOPICS FOR NEW CLINICAL PRACTICE GUIDELINES SELECTED?**

Developing an effective guideline starts with identifying topics that are relevant to patients, clinicians and healthcare providers, whilst avoiding industry influence. Topics can be important either because they are common in clinical practice, cause premature death or reduce quality of life or because there is uncertainty around optimal care [13]. ERBP identifies relevant new topics by consulting members of ERA-EDTA and representatives of the National Societies via annual surveys as well as providing the opportunity to freely suggest topics through electronic application forms. The Methods Support Team shortlists topics on an annual basis and presents these to the advisory board for prioritization based on consensus or majority vote. A summary report of all proceedings is kept on ERBP’s website for public viewing. Considering the breadth and depth of topics covered, as well as the time, effort and funds required for guideline production, a conscious attempt is made to avoid duplication of topics covered by other major guideline bodies (Table 1). ERBP’s guideline on transplantation for example purposefully covered kidney donor and

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**TABLE 1:** ERBP’s guideline on transplantation for example purposefully covered kidney donor and...
recipient selection as KDIGO had already covered care of the recipient after transplantation [14].

How is the guideline development group formed?

For each guideline project, a guideline development group is assembled to deliver the guideline. The advisory board appoints one of its members as the group’s chair and proposes an external co-chair. Together they select the other members of the team (Figure 2).

There is consistent empirical evidence that multidisciplinary groups tend to generate more balanced views [15] and broad international consensus that they are preferable to single-specialty groups [2, 9, 13]. ERBP aims to include a variety of methodological experts and clinicians, patients and other groups expected to be stakeholders in the guideline. To ensure balance of judgement and practicality of coordination, an average group includes between 12 and 15 participants. Clinical experts represent all disciplines relevant to the guideline [2]. For example, the development group for the guideline on hyponatraemia (in progress) comprises two endocrinologists, three intensivists and two internists in addition to five nephrologists. ERBP tries to identify interested participants through open invitations via ERA-EDTA as well as via national nephrology societies, and actively looks for experts by searching medical databases.

Conflict of interest, both intellectual and commercial, is a rightful concern for many people [4, 13, 16]. It is widely recognized that conflict of interest can misinform healthcare decision-makers, that guidelines should include disclosures of interest for members of the guideline development group and that guideline bodies should have policies in place to deal with potential conflicts [9]. Before ERBP awards development group membership, potential candidates have to declare all interests and activities that could result in a conflict of interest with development group activity. This is done using a standardized ‘Declaration of Interest’ document which includes all current, planned and past (i.e. dating back 2 years) commercial interests that are relevant to the scope of the guideline. ERBP acknowledges that ‘intellectual’ conflicts of interest can also exist and encourages open declaration. At all times, these documents can be consulted online at www.european-renal-best-practice.org. ERBP aims that chairs and co-chairs are free of all conflict of interest and other guideline development group members have only minimal if any conflicts. If granted panel membership, individuals are not excluded from discussions or decisions, regardless of their potential conflict. Decisions are made in consensus and if no consensus can be reached, individual votes of the guideline development group members are reported to ensure complete transparency of process.

Table 1. Other major guideline bodies producing renal guidelines

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Guideline body</th>
<th>Countries represented</th>
</tr>
</thead>
<tbody>
<tr>
<td>KDIGO</td>
<td>Kidney Diseases Improving Global Outcomes</td>
<td>Global</td>
</tr>
<tr>
<td>SLANH</td>
<td>Sociedad LatinoAmericana de Nefrologia e Hipertension</td>
<td>Latin America</td>
</tr>
<tr>
<td>KHA-CARI</td>
<td>Kidney Health Australia—Caring for Australasians with Renal Impairment</td>
<td>Australia, New Zealand</td>
</tr>
<tr>
<td>KDOQI</td>
<td>Kidney Disease Outcomes Quality Initiative</td>
<td>USA</td>
</tr>
<tr>
<td>CSN</td>
<td>Canadian Society of Nephrology</td>
<td>Canada</td>
</tr>
<tr>
<td>UK-RA</td>
<td>United Kingdom Renal Association</td>
<td>United Kingdom</td>
</tr>
</tbody>
</table>

FIGURE 2: Organizational chart ERBP. GDG: guideline development group.

HOW IS THE GUIDELINE DEVELOPED?

Determining which subtopics

One of the first tasks of the guideline development group is to identify which clinical problems or subtopics the guideline should cover. Decisions are based on the extent to which subtopics are considered a priority by the guideline stakeholders, which includes patients and clinicians, but also nursing staff.
and other related specialties. For this process, ERBP will apply and evaluate a Delphi-based consensus technique as part of the next two guidelines (on vascular access and advanced chronic kidney disease in the frail and elderly patient). As this is an on-going process, it will be reported on in a future publication.

**Determining which questions and which outcomes**

Within each subtopic one needs to identify which questions need answering to arrive at a particular recommendation [17]. Questions typically include identification of risk factors for a condition, accuracy of diagnostic tests, benefits and harms of various treatment options, importance of prognostic factors, etc. For example, to arrive at a recommendation that supports or discourages screening for chronic kidney disease, one needs to know if there are effective treatments to prevent poor outcomes in these patients, if there are tests that can accurately diagnose the condition, what are the potential harms of testing and who should be screened. At this stage, the group defines what outcomes are informative (e.g. health outcomes such as death and dialysis versus surrogate outcomes such as laboratory values) and what minimal clinical difference is important [17].

Most agree that trustworthy clinical practice guidelines are founded on high-quality systematic reviews of evidence [2, 9, 10, 18], including a systematic search for the evidence and its critical appraisal [19]. The steps of the development phase are discussed in the six sections below. Each step is illustrated in Figure 3 based on an example on routine ureteric stenting in kidney transplantation.

**Framing questions for systematic review**

Effective searching requires questions to be formulated specifically so that they can guide construction of electronic database search strategies. A well-accepted way to achieve this is by addressing each part of the acronym PICO(M).

- **P**—population or patient group: what specific (sub)group of patients does this recommendation apply to?
- **I**—intervention: what are the treatments or tests or risk factors being considered?
- **C**—comparator or control: what are the main alternatives?
- **O**—outcome: what are the outcomes that matter to patients and hence will drive our decision-making? What is their relative importance compared with each other?
- **M**—methodology: what study design is most valid to answer the question?

**Systematic search and study selection**

For each question, the key components of a systematic search include selecting which types of studies answer the question and searching multiple databases to identify evidence (Table 2) [23]. The systematic search procedures are planned, reviewed and conducted by the Methods Support Team because they require skills in systematically searching electronic databases and should be recorded, with results stored centrally to allow for easy future updating.

Once the searches are finalized, a member of the guideline development group and a member of the Methods Support Team both review all the abstracts of identified studies. If eligible, full-text versions of studies are retrieved and decisions about which studies should be included in the review are reached by consensus [23]. As of 2012, ERBP has started using an online service that helps the team execute these early stages of the evidence review [24].

**Data extraction, appraisal and summary**

For each included study, relevant data on study design, patient characteristics and outcomes are extracted and critically appraised for the reliability of results [25]. To guide the process of critical appraisal, ERBP uses the published questionnaires that are recommended by the Cochrane Collaboration [23]. As with study selection, for each question, both the Methods Support Team member and a guideline development group panellist complete the data extraction and critical appraisal.

Because duplicate data extraction adds tremendously to the time and effort required from guideline panellists, other guideline organizations have decided on having the systematic review process conducted exclusively by their methodological support groups [26, 27]. ERBP has decided to involve the guideline development group members in every step of the review process, convinced that a better understanding of the evidence and the methodology reduces the influence of bias through prior beliefs when it comes to formulating recommendations. To aid duplicate data extraction, resolution of discrepancies between reviewers and finally generation of consensus evidence tables, ERBP has customized and integrated an existing online data management system [28].

**Appraisal of body of evidence**

Recommendations are founded on the reliability of the evidence for benefits and harms of alternative management strategies. Consequently, in moving from reviewing the evidence from individual studies to making a recommendation, the guideline group needs to sequentially assess the quality of the ‘body of evidence’ (i.e. all studies together) for all predetermined outcomes [17]. This includes evaluating the reliability of results in the individual studies, consistency and precision of the results across studies, the extent to which results are directly applicable to the population targeted with the guideline and whether publication bias is likely to be an issue.

**Process of generating recommendations**

However, whether a guideline panel makes a recommendation for or against a management strategy and how strong that recommendation is likely to be, depends on more than evidence alone. Other factors include value judgements on the relative importance of specific outcomes and whether this might be variable among patients, whether benefits clearly outweigh the harms and ultimately whether the costs are worth the net benefits. To clarify what part is played by the quality of the evidence and what part by these other
considerations, two-tiered grading systems have been developed. Together with many other guideline bodies, within and outside of nephrology [17], ERBP has adopted the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) framework [29].

In GRADE, recommendations can be for or against a certain strategy, and can be strong (indicated by ‘1’ and communicated through the phrase ‘we recommend’) or weak (indicated by ‘2’ and communicated through the phrase ‘we suggest’). Recommendations can be supported by high (indicated by ‘A’) to very low (indicated by ‘D’) level evidence. The ultimate consequence is that a recommendation can be strong even when the quality of the evidence is very low (1D). For example, a few case reports on devastating harmful effects

associated with a treatment might be enough to prompt a strong recommendation against using that treatment, if a harmless alternative is available. Similarly, a recommendation can be weak even if the quality of the evidence is high (2A). For example, well-conducted randomized trials might show a particular treatment to improve one beneficial outcome, but at the cost of increasing the risk of another harmful outcome. Because patients with varying values and preferences make different choices, guideline development groups are likely to offer a weak recommendation in this case [20, 21].

For questions that cannot reasonably be answered by a systematic review of the evidence, but for which advice could still be quite helpful in practice, ERBP allows a separate ‘not graded’ category of guidance for clinical care, indicating that it is not supported by systematically synthesized evidence.

**Appraising implementability of recommendations**

Recommendations often fail to reach implementation in clinical practice. ERBP has decided to focus on facilitating implementation of guidelines in daily care.

As a first step, ERBP aims to optimize the wording of recommendations before sending out the guideline for review. For this purpose, ERBP has integrated the GuideLine Implementation Appraisal (GLIA) instrument into the guideline development process [22]. This tool primarily enables structured evaluation of factors such as executability (is it clear from the statement exactly what to do) and decidability (exactly under what conditions) of preliminary recommendations. In addition, the tool is designed to highlight other problems potentially hindering implementation, e.g. recommendations being inconsistent with clinicians’ existing beliefs or patients’ expectations. The appraisal is done by a panel of target guideline users external to the guideline development group. Panellists are acknowledged in the final document.

**HOW IS AN ERBP GUIDELINE WRITTEN AND PEER REVIEWED?**

For a guideline to be transparent, each recommendation must have a clear description of the potential benefits and harms, a summary of the relevant evidence and an explanation of the part played by values, opinion, theory and clinical experience in deriving the recommendation [2]. ERBP has developed a standard document template to reflect all three components. Guideline writing is overseen by a member of the Methods Support Team to guarantee maximal consistency in style and content.

Only a limited number of perspectives can be represented in a guideline development group. For this reason, the ERBP process invites input from additional external perspectives both from inside and outside of Europe and representing other specialties [30]. It is organized in two rounds. In a first round a targeted diverse set of reviewers, including scientific and clinical experts, organizations, agencies, patients and representatives of the public, is solicited. Reviewers are asked to comment on individual recommendations and the rationale regarding clarity, clinical usefulness and scientific accuracy using a standardized feedback form. All comments are collated and discussed among the guideline development group members, and a written record of the rationale for modifying or not modifying the guideline is kept with the guideline document. Reviewers are acknowledged in the final document. In a second round, the guideline is made available online for ERA-EDTA’s membership to provide comments through a standardized survey.

**WHAT ABOUT PATIENT PARTICIPATION?**

The Institute of Medicine recommends active patient participation in the process of guideline development as the

<table>
<thead>
<tr>
<th>Search hierarchy</th>
<th>Acronym</th>
<th>Database</th>
<th>Used to identify specific study design</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CDSR</td>
<td>Cochrane Database of Systematic Reviews</td>
<td>Cochrane systematic reviews</td>
</tr>
<tr>
<td>2</td>
<td>DARE</td>
<td>Database of Abstracts of Reviews of Effectiveness</td>
<td>Reviews of Effectiveness</td>
</tr>
<tr>
<td>3</td>
<td>CENTRAL</td>
<td>Cochrane central register of controlled trials</td>
<td>Randomized controlled trials</td>
</tr>
<tr>
<td>4</td>
<td>MEDLINE</td>
<td>Medical Literature Analysis and Retrieval System Online</td>
<td>Systematic reviews, randomized controlled trials, observational studies</td>
</tr>
</tbody>
</table>

**Table 2. Medical databases searched for evidence**

instrument to make guidelines more patient centred [2]. Unfortunately, patient participation is poorly studied, and opinions on how this best be done, differ [32]. ERBP is currently exploring alternative and complementary options for increasing patient involvement, while creating a framework that will allow evaluation of its effectiveness.

CONCLUSIONS

ERBP has made tangible steps towards rigorous guideline development methods in line with international standards and has prioritized transparency of processes. ERBP hopes these changes will not only further improve the quality of the guideline development process, but also enhance quality of care and improve outcomes of patients with kidney disease across Europe.

AUTHOR CONTRIBUTIONS

E.V.N. and A.C.W. researched and wrote and revised the manuscript. D.B., M.C.H., I.N. and S.V. researched and revised the manuscript. D.F. and W.B. conceived the idea for the paper and revised the manuscript.

ACKNOWLEDGEMENTS

We would like to acknowledge the members of the ERBP Advisory Board for their critical comments and the endorsement of this paper. These were, in addition to the co-authors of this paper: D. Abramowicz, J.B. Cannata, P. Cochat, A. Covic, K.U. Eckhardt, O. Heimburger, K. Jager, S. Jenkins, E. Lindley, F. Locatelli, G. London, A. MacLeod, A. Marti, G Spasovski, J. Tattersall, R. Vanholder, C. Wanner, A. Więcek and C. Zoccali.

CONFLICT OF INTEREST STATEMENT

Detailed declarations of interest (DOI) for members of ERBP are available at http://www.european-renal.bestpractice.org. Angela C. Webster has no relevant disclosures. The results presented in this paper have not been published previously in whole or part, except in abstract format.

(See related article by Denig and de Zeeuw. New renal guidelines; is more better? Nephrol Dial Transplant 2014; 29: 720–721.)

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Received for publication: 3.4.2013; Accepted in revised form: 20.8.2013