Clinical practice guidelines in infectious diseases

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INTRODUCTION

Clinical practice guidelines have been defined as ‘systematically developed statements to assist practitioner and patient decisions about appropriate healthcare for specific clinical circumstances’. They are intended to help practitioners to assimilate and implement the ever-increasing amount of scientific evidence and opinion on best current medical practice. Clinical practice guidelines should aim to improve the quality and appropriateness of care and possibly increase the cost-effectiveness of care. Furthermore, they can serve as an educational tool and as an instrument to reduce unjustified variations in clinical practice. For infectious diseases and antimicrobial therapy, another major goal of clinical guidelines is the control, or even reduction, of the level of antibiotic resistance. Clinical practice guidelines for infectious diseases were recommended by the European Union – initiated conferences in Copenhagen (1988) and Brussels (2001) – as an essential part of the measures to combat the problem of antimicrobial resistance. Scientific societies also supported the development of clinical practice guidelines.

Clinical practice guidelines preferentially rely upon the principles of evidence-based medicine, i.e. the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients. Hereby, they integrate individual clinical expertise with the best available external evidence and patient’s values and expectations. This implies that professional autonomy remains of the utmost importance in the application of a guideline to an individual patient. A guideline can never be specific enough to be applied in all situations and frequently a practitioner will be able to motivate the non-adherence to a guideline. Practice guidelines cannot be used as a cookbook, but merely offer a framework that is adjusted by clinical judgement. Therefore, guidelines are no substitutes for clinical evaluation and expertise nor can they replace expert witness opinions in litigation issues.

A high-quality evidence-based guideline requires a rigorous guideline development process by a multidisciplinary team of experts based upon a thorough systematic review of the literature with explicit grading of the guideline according to the level of the scientific evidence, and is followed by an external validation and quality appraisal. Such a systematic and transparent consensus development process linked directly to evidence from clinical studies guaranties both the validity of the guideline and a clarity in communication, so that the users of the guideline can act as responsible and informed practitioners. It also limits the risk of potential harm and non-intended use of the guideline.

GUIDELINE DEVELOPMENT

When analysing guideline development processes three main methods can be distinguished: informal consensus development, formal consensus methods and guidelines explicitly linked to evidence. Informal consensus development is the oldest and most common approach, coined by James Petrie, the former president of the Royal College of Physicians of Edinburgh, with ‘GOBSAT’ (Good Old Boys Sat Around the Table). Many guidelines are in fact developed by a group of experts that gather to write a guideline based upon their own opinion and experience. The composition of the group strongly
influences the outcome of the development process. The group members (some may even be self-appointed members) often share the same profession, read the same journals, regularly meet at other conferences and mutually reinforce their opinions. Moreover, small group processes may influence decisions when strong personal opinions dominate the development process, possibly resulting in ego-based guidelines instead of evidence-based guidelines. Thus, there are major sources of bias and guidelines produced in this manner are frequently of poor quality and lack adequate documentation of methods. This critique does not necessarily mean that these guidelines (or guides) are worthless. They can be very instructive and useful for clinicians and can be perceived as practical, familiar and realistic. Their flaws, mainly lack of methodological rigour and transparency, however, must be taken into account and it is often difficult for the user to assess how and on what basis the recommendations were derived.15,16 Practice guidelines developed by speciality societies are particularly vulnerable to these weaknesses. A survey of 431 guidelines from speciality societies showed that only 28% included a professional with another speciality (86% epidemiologist), 13% contained information on the systematic literature search and 18% used a grading of the strength of evidence.17 A typical example of the confusion these guidelines may create is given by the comparison of the practice guidelines on chronic obstructive pulmonary disease published by scientific societies from 15 countries.18

Formal consensus development uses a more systematic approach to assess expert opinion. In a consensus conference a broad-based panel listens to scientific data presented by experts, weighs the information and then composes a consensus statement that addresses a set of questions previously posed to the panel.14 This methodology to develop guidelines has several limitations as well. First, it is important to recognise who took the initiative for the conference, since it may reflect the overt or hidden goals, for example cost-containment instead of quality of care when organised by insurers or indirect marketing of a drug when organised by the industry. Other sources of bias are the composition of the panel, the selection of the literature and the experts, and the type of questions that were raised. The participants tend to be advocates of a certain view and participation in the conference allows them to be judge and jury to their advocacy.14 Small group processes within the panel again may have an influence on the final decision. The nature of a consensus conference may lead to imperfect scientific recommendations. Other sometimes quite sophisticated and complex methods, such as the Delphi method and the nominal group technique, have attempted to minimise the risk of major biases in the guideline development process, but so far it is unclear which formal consensus method is superior.19,20 Another type of a more or less formal consensus method, sometimes used for antibiotic prescription guides, is the organisation of a closed meeting of highly regarded experts that present and review previously raised questions. At the end they vote anonymously on the answers that were derived from the discussion. Finally, all participants approve a manuscript containing the literature review and the formal voting results. An example of this type of conference is the consensus paper on the management and prevention of severe Candidal infections.41 When looking at the voting results one realises that for the majority of the questions they reflect expert opinion not always supported by solid scientific data, for example differences in the choice of the antifungal agent or dosing according to underlying disease and severity of the inflammatory response. This type of consensus paper has its merits for guiding clinicians and raising unresolved issues, but its recommendations are less solid than evidence-based-type guidelines.

Evidence-based guideline development links guidelines directly to scientific evidence of effectiveness and appropriateness. A structured and transparent development process by a multidisciplinary development group based upon a thorough preferentially systematic review of the literature with a grading according to the strength of the scientific evidence is used. A consensus in the development group based on solid evidence is emphasised over expert opinion. The development process always includes an external validation with quality appraisal of the final guideline draft. The methodology such as described by the Scottish Intercollegiate Guidelines Network (SIGN, www.sign.ac.uk), and similar approaches by other scientific organisations, fulfils these requirements.42,43

**GUIDELINE DEVELOPMENT PROCESS**

An evidence-based guideline development process typically distinguishes five steps:12,15

1. The identification and refinement of the subject area.
2. The selection of the development group.
3. The search for and critical appraisal of the evidence in the literature.
4. The translation of the evidence into a clinical practice guideline and grading of the strength of the recommendation according to the level of evidence.
5. External review and quality appraisal of the guideline and scheduling of the updating.

To identify the subject for a guideline, priority is usually given to topics that are clinically relevant (volume, variation in practice, risks for patient, costs) and for which sufficient evidence is available. The subject must then be narrowed (e.g. not ‘treatment of pyelonephritis’ overall but ‘antibiotic therapy of uncomplicated community-acquired pyelonephritis in immunocompetent women’, excluding patients...
with underlying disease, obstruction, surgery, urinary catheters, etc.). The purpose of the guideline must be clearly stated. Next and most critical, a guideline development group is selected. This multidisciplinary group consists of at least six and, for practical reasons, not more than 12 to 15 methodological and mostly clinical experts from related disciplines including delegates from scientific and professional societies. The roles of the group leaders – i.e. to supervise the process and keep in mind the final goal, and the group members to interpret the evidence, add clinical expertise and watch practicalities – are well understood from a first introductory meeting.

A systematic literature search using preappraised sources (such as existing evidence-based guidelines, systematic reviews in e.g. the Cochrane Library, meta-analyses, etc.) and databases with the original primary literature (such as Medline or Embase) is done and the search strategy is described explicitly. Randomised controlled trials are preferred in therapy guidelines, but if unavailable or insufficient the search can be extended to observational studies. Critical appraisal of the methodological quality of the evidence and an appreciation of its relevance, validity and applicability is performed using standardised checklists. An evidence table incorporating a description of the validated studies is then compiled and the evidence is summarised in a first guideline draft in which the levels of evidence are clearly categorised. The members of the development group evaluate the volume and consistency of the evidence and integrate it with their clinical expertise and with feasibility issues to create a graded recommendation in multiple rounds.

A distinct and specific feature of infectious diseases guidelines is that local epidemiology and resistance data must be taken into account. This may lead to a different appraisal of the evidence in foreign guidelines on the treatment of the same infectious disease.

The grade of the recommendation reflects the strength of the evidence on which it is based. Unfortunately, different grading systems are being used (e.g. revised SIGN grading; Infectious Diseases Society of America – United States Public Health Service grading system, etc.) leading to confusion for the inexperienced reader. When strong evidence from clinical trials is lacking expert opinion and extrapolation from other patient groups, pathophysiological insights or animal experiments can be used. This must be clearly recognisable for the guideline users as such in the grading. Once the final guideline manuscript is approved by the development group, an external review with quality appraisal is initiated to ensure validity, clarity and applicability. This review process should include an expert in the clinical context, an expert in systematic review and guideline development, and potential users of the guideline. More and more evidence-based guideline developers include further peer review via an open meeting where all medical societies involved are invited. Frequently, guidelines are pretested by a limited group of practitioners before general dissemination and implementation of the guideline. Finally an updating of the guideline must be scheduled.

The AGREE instrument (Appraisal of Guidelines Research and Evaluation in Europe collaboration), supported by the 5th framework of the European Union and published in June 2001 (www.agreecollaboration.org), offers an internationally accepted methodology to evaluate the development process (not the content). It is a checklist that allows the individual practitioner or organisation to make an informed judgement about the methods that were used to develop a guideline and to assess the overall quality of the guideline and the recommendations it contains. Six domains are covered by 23 key items: scope and purpose, stakeholder involvement, rigour of development, clarity and presentation, applicability, and editorial independence.

A review of 279 guidelines published from 1985 to 1997 shows that 51% of the guidelines adheres to the methodological standards for guideline development and format, 34% for identification and summary of the evidence and 46% for the formulation of recommendations. There was improvement over time but the identification, evaluation and synthesis of the scientific evidence remained weak. The clinical guideline development project of the Belgian Antibiotic Policy Coordination Committee (BAPCOC) section hospital medicine, which started two years ago, strictly adheres to an evidence-based methodology. It engaged two part-time scientific collaborators to act as group leaders, perform the systematic literature search and summarise the evidence in a first guideline draft.

Active involvement of several of the national scientific societies concerned, according to the topic, was obtained. The selection of the topics was decided by a steering committee taking into consideration priorities that arose from the analysis of the linked minimal clinical data (using All Patients Refined Diagnostic Related Groups; APR DRGs) and minimal financial data. This reporting is legally imposed in all Belgian hospitals and provides detailed data on the use of resources (including choice and duration of medication) and the precise diagnosis for each hospitalisation. Great variation in clinical practice, overuse and underuse, inappropriateness and unjustifiable costs and differences between hospitals are striking features of this type of analysis. This minimal data analysis will also allow evaluation of the impact of a future guideline on daily clinical practice. The ‘Stichting Werkgroep AntibioticaBeleid’ (SWAB) in the Netherlands started in October 1996. It has a similar structure (scientific staff, steering committee and extended expert group) and aims to develop national guidelines for antibiotic use in hospital practice. SWAB also moves towards a more explicit grading of the evidence and the recommen-
dations and has departed from the more narrative style of previous publications.

**DISSEMINATION, IMPLEMENTATION AND EVALUATION**

The methodology for guideline development was gradually developed and adopted by the medical scientific community over the last decade. Much more research is still needed in the dissemination, implementation and evaluation processes of well-conceived guidelines. Passive methods of dissemination and implementation of guidelines, such as publication in a scientific journal or mailings, rarely lead to changes in professional behaviour. Multifaceted interventions are supposed to be more successful and the choice of the strategies depends upon available resources, perceived barriers and research evidence about effectiveness and efficiency of different approaches. Academic detailing (educational outreach), local adaptation by a multidisciplinary antibiotic management team, small-group interactive sessions, computer-assisted care and audit and feedback appeared to be useful implementation methods (Cochrane review). The Belgian experience concerning the change in the reimbursement of perioperative antibiotic prophylaxis indicates that, apart from professional, organisational, social and regulatory interventions, financial incentives can have a strong impact on achieving guideline implementation. It is of utmost importance to identify the reasons why physicians do not follow clinical practice guidelines. Three domains of barriers to physician’s adherence are recognised in general: lack of knowledge, attitude and external barriers. Lack of awareness, of accessibility or of familiarity with guidelines are often cited by physicians as a main reason for non-adherence. An assessment of the knowledge of guidelines for the prevention of infective endocarditis underscored this deficiency. Lack of agreement with guidelines in general or with a specific guideline and lack of outcome expectancy (risk for patient) also determine physician’s attitudes. Physicians with a longer clinical experience and possibly more settled attitudes may be more likely not to follow a guideline. Patient factors and environmental factors (general practitioner involvement, financial barriers, hospital bed management policy, etc.) also may compromise adherence. A survey of Italian physicians illustrates the traditional perception of practice guidelines. They declared that personal experience, opinions of colleagues and other sources of information were more useful, that guidelines are not transferrable to the individual patient or local situation and threaten the doctor’s autonomy, that guidelines are externally imposed for cost-containment reasons only and that they are administrative rather than informative or educational. Furthermore, there was no enthusiasm for multidisciplinary involvement. Other surveys, however, revealed that physicians are generally positive and confident in guidelines developed by physicians and that acceptability of the format and medium for guideline presentation should be pretested. Finally, evaluation of the impact of the guideline must be planned. It assesses the efficacy of the guideline to ensure that the intended changes in practice and outcome were produced. Audit is the most effective way of doing this. Feedback to practitioners enhances the impact of the evaluation process.

**GUIDELINES IN INFECTIOUS DISEASES**

Guidelines are considered an essential part of the measures to combat antimicrobial resistance. There is general agreement that they can improve both the quality and the cost-effectiveness of care. Many types of interventions to implement changes in antibiotic prescriptions have been proposed. A distinction is made between educational, supportive and more restrictive methods. To a lesser or greater extent, all of them can have an influence on prescription behaviour, but good data that determine the best type of intervention for specific purposes are scarce. An EPOC (Effective Practice and Organisation of Care) evaluation protocol for systemic review of the literature on this topic is currently being performed. During a workshop at the European Union Conference in Brussels it was concluded that a large body of evidence from databases such as the Cochrane database indicates that the following interventions have a significant effect on healthcare provider behaviour: education, guidelines, outreach visits and academic detailing, audit and feedback. Of these, outreach visits and academic detailing appear to be the most consistently effective and several studies confirm their feasibility and safety in the infectious diseases setting. The infectious diseases consultation service enhanced the appropriateness of the clinical management and favourably influenced the outcome of patients with severe infections. The European Study Group on Antibiotic Policy recommended the establishment of a rational antibiotic policy as the key issue for better care of patients and the combat of antimicrobial resistance. A national expert committee on antibiotic policy (such as BAPCOC in Belgium) should be established in each country to establish national strategies for creating and auditing national antibiotic policies, including the development of regional clinical practice guidelines. Each healthcare institution should have a therapeutics committee to develop a local antibiotic policy based on national guidelines. The Belgian government is now planning to start with the funding of local antibiotic policy committees in the Belgian hospitals. Such a multidisciplinary antimicrobial management team is considered...
to be the most appropriate structure to adapt, implement and evaluate infectious diseases guidelines and interventions in hospitals according to local epidemiology, antibiotic consumption patterns and antibiotic resistance data, as was stated in the workshop report of the 2001 European Union-initiated Brussels Conference.

**CONCLUSION**

High-quality clinical practice guidelines rely upon a rigorous guideline development method using a systematic review of the scientific evidence and an explicit linkage between the level of evidence and the strength of recommendation. Implementation of practice guidelines requires timely and multifaceted interventions and evaluation of the impact of the guideline should be undertaken. Infectious diseases guidelines must meet the international standards of guideline quality but, most importantly, they also require the integration of local epidemiology and resistance data. A multidisciplinary antimicrobial management team in the local hospital seems essential for interpretation, local translation, and implementation of infectious diseases guidelines.

**NOTE**

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**REFERENCES**


