Port J Nephrol Hypert 2011; 25(4): 249-252
Advance Access publication 14 November 2011

Clinical practice guidelines and the practice of nephrology

António Vaz Carneiro, MD, PhD, FACP

Center for Evidence Based Medicine, University of Lisbon School of Medicine. Portugal.

Received for publication:	07/11/2011
Accepted:	10/11/2011

The modern physician does not seem to be able to escape clinical practice guidelines (CPGs). These publications show up with increasing frequency in most major clinical journals, taking up more and more space. A search in Medline over the past 10 years using the keyword "practice guidelines" will return thousands of articles.

A recent definition of CPGs states that they are "*statements that include recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options*." (Institute of Medicine. Clinical Practice Guidelines We Can Trust. Washington, DC: National Academies Press. 2011)

The ultimate impact of CPGs is on patient outcomes, and there is abundant evidence of their benefits. For example, it was recently shown that in a Swedish registry of patients with ST-elevation acute myocardial infarction (SWEDEHEART/RIKS-HIA), there was between 1996 and 2007 an increase in the prevalence of evidence-based treatments, with a concomitant decrease in 30-day and 1-year mortality. This benefit was sustained during a long-term follow-up[1].

As such, CPGs seem to address the needs of four major stakeholders in any National Health System: health professionals, health managers/administrators, politicians and patients.

- For health professionals, CPGs give access to scientific information relevant to a disease or patient, allow clear recommendations for practice, may be used as a quality assurance programme and may improve clinical work through diminished practice variation and implementation of cost-effective measures.
- For health managers/administrators, CPGs allow a more solid management, better local policies, with establishment of clinical standards and cost-containment strategies that do not sacrifice quality.
- For high level policy decisions, CPGs can contribute as a basis for a more robust decision-making process, for example in comparing different policies.
- Finally, for patients, CPGs are quality assurance instruments that help the practice of an updated medicine and produce desired patient-specific outcomes.

Ideally, CPGs are supported by the best and most relevant clinical evidence available at the time of their design. In conceptual terms, quality of evidence is defined as the degree of confidence in the precision of the estimated clinical effect, and relevance as the capacity to answer the original clinical questions stated by the CPG[2]. This approach is absolutely essential, since it is the only one that can lend credibility to its contents – a baseline condition for its practical implementation.

Because there are several concerns about the intrinsic quality of the evidence that support guideline recommendations – lack of clarity about who shapes the recommendations (expert opinion or evidence), conflict of interests among authors, or methodological issues (types of patients included or excluded, for example) – a recently published statement paper has addressed the issues of conflicts of interest,

type of clinical recommendations, grading system for the quality of evidence and strength of recommendations, update process and dissemination of the conclusions[3].

Supporting this approach, a widely accepted set of standards has been recently published (Institute of Medicine. Clinical Practice Guidelines We Can Trust. Washington, DC: National Academies Pr; 2011) that allows a careful analysis of the trustworthiness of CPGs (Table I).

Table I

Set of standards for a trustworthy CPG (IOM 2011)

- Has an explicit description of development and funding processes that is publicly accessible
- Follows a transparent process that minimizes bias, distortion, and conflicts of interest
- Is developed by a multidisciplinary panel comprising clinicians; methodological experts; and representatives, including a patient or consumer, of populations expected to be affected by the guideline
- Uses rigorous systematic evidence review and considers quality, quantity, and consistency of the aggregate of available evidence
- Summarizes evidence (and evidentiary gaps) about potential benefits and harms relevant to each recommendation
- Explains the parts that values, opinion, theory, and clinical experience play in deriving recommendations
- Provides a rating of the level of confidence in the evidence underpinning each recommendation and a rating of the strength of each recommendation
- Undergoes extensive external review that includes an open period for public comment
- Has a mechanism for revision when new evidence becomes available

The need for a rigorous approach to guideline development is well justified by the fact that some of the recently published clinical guidelines from well-known professional societies – infectious diseases[4] and cardiology[5] – are lacking good evidence to support their recommendations.

To overcome these methodological problems, several professional groups have published technical papers on the steps to be taken in order to achieve the best possible results, i.e., building a sound evidence-based instrument for clinical practice. One of the best examples of this approach is the papers issued by the U.S. Preventive Services Task Force (USPSTF).

The USPSTF is an internationally recognised, independent panel of American experts in primary care that makes evidence-based recommendations to guide clinical preventive services[6,7]. It adheres to a series of rigorous steps to develop its two different types of clinical recommendations: clinical practice guidelines and clinical guidance statements. These steps include selection of topics, determination of the scope of the topic, review of the evidence for clinical recommendations and development, review, and approval of those recommendations[3].

As an example of a major methodological basis for GPC development, in selecting a topic, the USPSTF considers prevalence of the condition, its effect on morbidity and mortality, whether effective health care is available, if there are areas of uncertainty, evidence that current performance does not meet best practices, the cost of the condition, clinical relevance and the likelihood that evidence is available to develop the recommendations.

One other major aspect of methodological quality is the grading system for the quality of evidence and strength of recommendations used by USPSTF. The need for this type of hierachy stems from the fact that there are different types of evidence that can serve as a basis for any recommendation and this fact should be acknowledged by the end-users intending to implement it. For example, the recommendation of modulating microalbuminuria and albuminuria in diabetics has a much better evidence base[8,9] than controlling the phosphate with phosphate binders in patients with CKD[10].

There are several grading systems, but the most widely adapted is the GRADE System (http://www.gradeworkinggroup.org) and Table II shows the adaptation of this system to the ACP guideline development[3]. This same grading system has also been adapted by the Kidney Disease: Improving Global Outcomes (KDIGO) group[11].

These approach is not without problems, because there are characteristics of chronic kidney disease itself (and CKD patients) that need to be considered in any grading system[11]: CKD is most of the time a silent disease with a chronic course and its clinical outcomes of interest are complex (progression to kidney failure, development or progression of CVD, problems with quality of life and development or progression of complications). To complicate things, there is a relatively small number of high-quality studies examining critical clinical outcomes in populations with CKD as well as RCTs that concurrently and definitively examine all important clinical outcomes and harms.

Table II

American College of Physicians guideline grading system

Grade of Recommendation	Benefit Versus Risks and burdens	Methodological Quality of Supporting Evidence	Interpretation	Implications
Strong recommendation; high-quality evidence	Benefits clearly outweigh risks and burden or vice versa	RCTs without important limitations or overwhelming evidence from observational studies	Strong recommendation; can apply to most patients in most circumstances without reservation	For patients, most would want the recommended course of action and only a small proportion would not; a person should request discussion if the intervention was not offered. For clinicians, most patients should receive the recommended course of action. For policymakers, the recommendation can be adopted as a policy in most situations.
Strong recommendation; moderate-quality evidence	Benefits clearly outweigh risks and burden or vice versa	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies		
Strong recommendation; low-quality evidence	Benefits clearly outweigh risks and burden or vice versa	Observational studies or case series	Strong recommendation, but may change when higher-quality evidence becomes available	
Weak recommendation; high-quality evidence	Benefits closely balanced with risks and burden	RCTs without important limitations or overwhelming evidence from observational studies	Weak recommendation; best action may differ depending on circumstances or patients' or societal values	For patients, most would want the recommended course of action but some would not–a decision may depend on an individual's circumstances. For clinicians, different choices will be appropriate for different patients, and a management decision consistent with a patient's values, preferences, and circumstances should be reached. For policymakers, policymaking will require substantial debate and involvement of many stakeholders.
Weak recommendation; moderate-quality evidence	Benefits closely balanced with risks and burden	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies		
Weak recommendation; low-quality evidence	Uncertainty in the estimates of benefits, risks, and burden; benefits, risks, and burden may be closely balanced	Observational studies or case series	Very weak recommendations; other alternatives may be equally reasonable	
Insufficient	Balance of benefits and risks cannot be determined	Evidence is conflicting, poor quality, or lacking	Insufficient evidence to recommend for or against routinely providing the service	For patients, decisions based on evidence from scientific studies cannot be made; for clinicians, decisions based on evidence from scientific studies cannot be made; for policymakers, decisions based on evidence from scientific studies cannot be made.

What is happening in the nephrology world and who is doing what?

The best know initiative is the Kidney Disease Improving Global Outcomes (KDIGO). It defines itself as "an independently incorporated non-profit foundation governed by an international board of directors with the stated mission to improve the care and outcomes of patients with kidney disease worldwide, through promoting coordination, collaboration, and integration of initiatives to develop and implement clinical practice guidelines." (www.kdigo.org).

KDIGO is one of the best examples of a well-organised endeavour to draw up high quality, evidence-based CPGs. It has evolved from other initiatives and has become a global effort in nephrology – most of its recommendations are supported by external renal organisations. For example, the grading system has also been reviewed by representatives for Caring for Australasians with Renal Impairment, United Kingdom Renal Association, European Best Practice Guidelines, Canadian Society of Nephrology, and Kidney Disease Outcomes Quality Initiative[11].

Some KDIGO publications include, for example, Prevention, Diagnosis, Evaluation and Treatment of Hepatitis C in Chronic Kidney Disease (doi:10.1038/ncpneph0953) and Diagnosis, Evaluation, Prevention and Treatment of Chronic Kidney Disease related Mineral and Bone Disorders (Kidney International Suppl 113, 2009). It plans to publish in the near future guidance on acute kidney injury (AKI), glomerulonephritis, hypertension in CKD, anemia in CKD, classification and management of CKD, lipids in CKD – to name just a few.

These KDIGO CPGs are methodologically very strong, since they involve a series of steps that assure their quality and evidence base: topic selection and order of priority, followed by conferences on controversies. Work group selection and avoiding conflicts of interest comes next. The guideline development process includes evidence rating, public review process, publication dissemination and implementation, as well as updating.

For example, the criteria for topic selection includes: 1) burden of illness based on prevalence and scope of the condition or clinical problem, 2) amenability of a particular condition to prevention or treatment and expected impact, 3) existence of a body of evidence of sufficient breadth and depth to enable the development of evidence-based guidelines, and 4) potential of guidelines to reduce variations in practices, improve health outcomes, or lower treatment costs. These criteria constitute an explicit and clear order of priority basis for CPG development in nephrology.

After reviewing some of the issues concerning guideline-based nephrology practice, how can we sum up this matter?

I think that the message is twofold: firstly, modern clinical practice needs good quality guidelines as a basis for medical decision making. And secondly, they need to be evidence-based, in order to maintain credibility as a basis for implementation.

Their practical use will be difficult and involve a significant number of stakeholders, of which nephrologists will have to be the leading force. Clinical practice guidelines are here to stay, so we should use them as a basis for medical decision making.

Conflict of interest statement. None declared.

References

1. Jernberg T, Johanson P, Held C, Svennblad B, Lindback J, Wallentin L. Association between adoption of evidence-based treatment and survival for patients with ST-elevation myocardial infarction. JAMA 2011;305:1677-1684

2. Roque A, Bugalho A, Carneiro AV. Manual de elaboração, disseminação e implementação de normas de orientação clínica. 1st ed. Lisboa: FML; 2007

3. Qaseem A, Snow V, Owens DK, Shekelle P. The development of clinical practice guidelines and guidance statements of the American College of Physicians: summary of methods. Ann Int Med 2010;153:194-199

4. Lee DH, Vielemeyer O. Analysis of overall level of evidence behind Infectious Diseases Society of America practice guidelines. Arch Intern Med 2011;171:18-22

5. Tricoci P, Allen JM, Kramer JM, Califf RM, Smith SC, Jr. Scientific evidence underlying the ACC/AHA clinical practice guidelines. JAMA 2009;301:831-841

6. Barton MB, Miller T, Wolff T et al. How to read the new recommendation statement: methods update from the U.S. Preventive Services Task Force. Ann Int Med 2007;147:123-127

7. Guirguis-Blake J, Calonge N, Miller T, Siu A, Teutsch S, Whitlock E. Current processes of the U.S. Preventive Services Task Force: refining evidence-based recommendation development. Ann Int Med 2007;147:117-122

8. Strippoli GF, Craig M, Deeks JJ, Schena FP, Craig JC. Effects of angiotensin converting enzyme inhibitors and angiotensin II receptor antagonists on mortality and renal outcomes in diabetic nephropathy: systematic review. BMJ 2004;329:828

9. Hemmelgarn BR, Manns BJ, Lloyd A et al. Relation between kidney function, proteinuria, and adverse outcomes. JAMA 2010;303:423-429.

10. Adragão T, Vaz Carneiro A, Ferreira A, Frazão JM, Strippoli G, Vinhas J. Position statement of the Portuguese Society of Nephrology on the treatment of chronic kideney disease-related mineral and bone disorders. Port J Nephrol Hypert 2009;23:31-36

11. Uhlig K, Macleod A, Craig J et al. Grading evidence and recommendations for clinical practice guidelines in nephrology. A position statement from Kidney Disease: Improving Global Outcomes (KDIGO). Kidney Int 2006;70:2058-2065

Correspondence to:
Prof. António Vaz Carneiro, MD, PhD, FACP
Faculty of Medicine, University of Lisbon
Head, Center for Evidence Based Medicine
Av. Prof. Egas Moniz
1649-028 Lisboa
PORTUGAL
E-mail: avc@fm.ul.pt