Evidence-Based Clinical Practice Guidelines: What is the Evidence?

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Evidence-based medical practice has a long history reaching back to the 17th century, but it has become systematically applied particularly in the last 40 years. Five cardinal tenets underpin EBMP [2]: Recognition of the patient's problem; construction of a structured clinical question; a search for the best possible evidence relevant to the question; critical appraisal of the evidence; and most importantly, ethical integration of the best evidence, taking into account the particular contexts and the clinical circumstances as well as benefits, costs and risks. The first two of these tenets lie within the classic realm of medical education, the third within the burgeoning field of informatics. It is the third and fourth areas that are addressed by clinical practice guidelines. The fifth tenet, implementation, stresses the importance of evidence-based medical practice, but also its limitations. As Vashitz and his colleagues reveal, a true physician can never be a medical technician, rigidly implementing "recipes"; he or she must always be a skilled exponent of a long and proud professional tradition in which the individual patient, and not population statistics, remains central. The tools of EBPM are varied and include systematic reviews, narrative reviews, health technology assessments, meta-analytic reviews, and audits. Each of these can aid the understanding of current knowledge in different ways, but their quality is variable and should be carefully evaluated. Reviews are only as good as the original studies upon which they are based, and syntheses of reviews (meta-analyses) therefore also require careful scrutiny. They are not infallible [2]. CPGs are based on syntheses and therefore must be based upon reliable, good quality reviewed evidence, and then must be properly constructed. This is no simple task.

Clinical Practice Guidelines are systematically developed statements that aim to assist physicians and patients in obtaining the best possible health outcomes [9]. They are by their nature consensus documents [10], blurring differences of interpretation and opinion. Such differences may reveal themselves later via variable implementation decisions ("non-adherence to CPGs") that, it must be clearly stated, may be entirely legitimate and appropriate in...
the increasing number and popularity of clinical practice guidelines and the reasonable assumption that better CPGs will lead to better results [12], their evaluation for quality and applicability has itself become a subject of importance. The Appraisal of Guidelines Research and Evaluation Project ("AGREE") [12,13] lists 17 separate items that contribute to CPG quality, while the WHO [2], the Australian National Health Service Medical Research Council (NHMRC) [2] and others have drawn up standards for CPG development. Many of these standards have been referred to above. One of the most interesting, however, in the light of Vashitz's paper, is the call for CPGs to be contextualized with regard to the strength of evidence [12]. This in effect calls for every CPG to take into account the flexibility required if the evidence is weak or non-rigorous evidence, as well as the clinical context in which the physician practices. CPGs are just that – guidelines, not regulations, rules or laws. CPGs must be available in practical formats; paper-printed volumes gathering dust on shelves are unlikely to be consulted whereas attractively designed posters and charts and electronic formats may be more accessible at the time and point of need. Dissemination, physician and patient education, awareness, and reminders are all important for practical results to be achieved. In this respect, the seminal work being done by organizations such as Britain's National Institute for Health and Clinical Excellence (NICE), the U.S. Institute of Medicine (IOM) and National Guideline Clearinghouse (NGC), Australia's NHMRC, and others, should be noted.

And yet for all this, medical practice not concordant with evidence-based CPGs remains ubiquitous. Why? The reasons for “non-adherence” to CPGs and the non-implementation of evidence-based medicine are many and varied, and have been summarized in a differential diagnostic flow chart by Cabana et al. [10]. Physician knowledge may be limited by time constraints, too much information or complexity, and poor accessibility. Physicians may not agree with a particular CPG or with CPGs in general [14]. Often physicians have seen the attempt to introduce CPGs as a challenge to autonomy and their use as a reversion to rigid “cookbook” medicine. Lack of motivation has been particularly studied and the effect of demographic, economic, personal, geographic, practice mix and load, and educational factors have all been reported [15]. Patient-related factors are also influential. Organizational factors such as lack of support, lack of resources and staff, and lack of protected funded time may all limit the implementation of CPGs in real-life settings. Lastly, there may be fears of increased malpractice exposure [16].

So what is to be done? It is recognized that there are no magic solutions for improving implementation of CPGs and that changing physician behavior is a daunting challenge. The evidence for the efficacy of different strategies is limited and often not generalizable [10]. Most interventions are effective under some circumstances and none are effective under all circumstances [8]. Sustainability is problematic [8]. No intervention as a single maneuver has been shown to be effective but multi-faceted approaches have had better success [9,17-19]. The process should be carefully planned, preferably by a dedicated group such as an evidence-based Practice Support Group [16], and its success evaluated. Predisposing, enabling and reinforcing phases are all important. Among the latter, clinical audit, feedback and physician profiling may be helpful. In recent years, much interest has been shown in computer-aided tools such as the so-called Clinical or Computer Decision Support Systems (CDSS). These may improve prescription habits but overall they are as yet unproven [9].

The implementation of CPGs may lead to undesirable consequences. Of these, two should be particularly emphasized. The measurement of quality assurance indexes based on uncritical and rigid interpretation of CPGs can lead to over-bureaucratization and the phenomenon of the computer-screen doctor. Excessive time and effort demands caused by intrusive QAI measurements may be detrimental to the patient-doctor relationship, which is at the heart of true quality in medicine. This of course is hard to measure in value-based QAI systems, and so is ignored. The second danger is the adoption of the CPG as a medico-legal standard in malpractice and negligence cases. It must be emphasized that clinician experiential knowledge and skill, and patient concerns, are at the heart of medical care. The skilled physician knows how to blend these with scientific evidence, and his experience and judgment, not statistics, are the crucial factor. Thus, CPGs should not become de facto legal

WHO = World Health Organization

QAI = quality assurance indexes
Epileptic seizures are a common and poorly understood comorbidity for individuals with primary brain tumors. To investigate peritumoral seizure etiology, Buckingham et al. implanted human-derived glioma cells into severe combined immunodeficient mice. Within 14–18 days glioma-bearing mice developed spontaneous and recurring abnormal electroencephalogram events consistent with progressive epileptic activity. Acute brain slices from these mice showed marked glutamate release from the tumor mediated by the system x−c cystine-glutamate transporter (encoded by SLC7A11). Biophysical and optical recordings showed glutamatergic epileptiform hyperexcitability that spread into adjacent brain tissue. The authors inhibited glutamate release from the tumor and the ensuing hyperexcitability by sulfsalazine (SAS), a U.S. Food and Drug Authority-approved drug that blocks system x−c. We found that acute administration of SAS at concentrations equivalent to those used to treat Crohn’s disease in humans reduced epileptic event frequency in tumor-bearing mice compared with untreated controls. SAS should be considered as an adjuvant treatment to ameliorate peritumoral seizures associated with glioma in humans.

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Monoclonal antibodies against influenza viruses

An important goal in public health is the development of a universal influenza vaccine. Broadly neutralizing antibodies against group 1 influenza A virus have been described; however, a broadly neutralizing antibody against group 2 viruses has not. Ekiert and team (Science 2011; 333: 843) describe the isolation and characterization of a human monoclonal antibody, CR8020, with broadly neutralizing activity against group 2 viruses, which recognizes a region distinct from that recognized by the group 1 antibodies. In a separate study, Corti et al. (p. 850) report the isolation of an antibody from an influenza-infected individual that shows neutralizing activity against both group 1 and group 2 influenza A viruses. The antibody binds to a conserved region in the influenza hemagglutinin. Administration of the antibody protected both mice and ferrets against infection with a group 1 or group 2 influenza A virus.

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