

How useful are laboratory practice guidelines?

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ABSTRACT

Clinical practice guidelines (CPGs) relating to laboratory diagnostic testing are increasingly produced with the aim of standardizing practice and improving patient care based on the best available evidence. However, the production of a CPG is merely the first step in the process of getting evidence into practice, to be undertaken by laboratories and other stakeholders. This process should evaluate the information provided in the guidelines on laboratory tests, devise a strategy for implementing the CPG or the laboratory aspects of the CPG and finally, once implemented, assess the impact of the CPG on clinical practice, patient outcomes and costs of care.

The purpose of CPG evaluation by the laboratory is to determine whether sufficient information is provided on the particular test recommended. CPGs may not always be written with the involvement of a laboratory specialist and this underlies the paucity of relevant information in some national guidelines. When laboratory specialists are involved, CPGs can provide practical information which supports local laboratories as

well as clinicians in the implementation and appropriate use of recommendations.

Implementation of CPGs is an often neglected area that needs attention and thought. There are many barriers to successful implementation, which may vary at local level. These need to be identified early if CPGs are to be successfully adhered to. The effectiveness of CPGs also needs to be audited using process and health outcome indicators. Clinical audit is an effective tool for assessing adherence to recommendations and for measuring the impact and success of the CPG.

INTRODUCTION

Clinical practice guidelines (CPGs) relating to laboratory diagnostic testing are increasingly produced with the aim of standardizing practice and improving patient care, based on the best available evidence. There are relatively few guidelines dealing purely with the laboratory medicine aspects of patient care and the majority of laboratory related recommendations are embedded in CPGs. Unfortunately, these are often inadequately detailed to be useful for laboratories (1). Therefore laboratory medicine specialists should be more actively involved in the production of clinical guidelines to ensure that advice is given about the appropriate utilization of laboratory tests.

It is important to remember that the production of a CPG is merely the first step in a larger process that needs to be undertaken by laboratories and other stakeholders. The next step is implementation. This process, firstly, should evaluate and assess the quality of the guideline in order to ensure that a sufficient level of information is provided. Secondly, the process for guideline implementation needs to be planned with due consideration given to local barriers that may prevent guideline adoption. CPG production is a lengthy process, but largely futile

if efforts are not made to ensure adoption, dissemination and implementation. Finally once implemented, the effectiveness of the CPG needs to be evaluated. This may be through clinical audit, which is an essential tool to evaluate uptake, impact on practice, patient outcome and resource utilization.

An understanding of this process is important as it underpins good laboratory practice and forms the basis of practicing evidence-based laboratory medicine. Below we highlight key aspects of this three-step process of evaluation, implementation and audit of CPGs.

HOW SHOULD LABORATORY TEST ADVICE BE INCLUDED IN CPGs?

Guidelines are typically produced by specialist groups, often national or international societies, frequently involving only single clinical specialties. Whilst the classification of the hierarchy of evidence is well described, there appears to be no standardized approach to reporting guidelines (see Kahn *et al*, this issue). Both these factors hinder the development of good laboratory based guidance as laboratory medicine specialists are rarely included in writing committees and the evidence base for diagnostic tests is largely observational with few randomized trials assessing the impact of the diagnostic test on clinical pathways. Only observational evidence supports, for example, the use of glycated haemoglobin in the diagnosis of diabetes and that of troponin in acute coronary syndrome.

There is clearly a need to ensure that good diagnostic test guidance is included in CPGs. This has been achieved for a few disorders that are managed by a number of different disciplines and where guidelines have been written by multidisciplinary teams. Successful examples of this co-operative approach include work by the European Atherosclerosis Society (EAS) in

association with the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) which has resulted in the development of two consensus papers (2, 3) and more recently, a joint Consensus Panel which has written guidelines for lipid testing in the management of dyslipidemia and cardiovascular risk (4). Another example would be the recent British Thyroid Cancer guidelines, written by a range of clinicians and laboratory medicine specialists, and providing detailed information on the appropriate use of thyroglobulin and calcitonin assays (5). There are also inter-society collaborations whereby a practice guideline primarily developed by a laboratory medicine organization is adopted by a clinical society. For example, the Diabetes Mellitus guideline of the National Academy of Clinical Biochemistry (NACB) (6) has been adopted and published as an officially endorsed recommendation by the American Diabetes Association (7). Joint development and endorsement of CPGs by clinical and laboratory medicine societies is complementary and safeguards that the most appropriate and relevant advice is provided for the use and interpretation of laboratory results.

Similar to any other types of guidelines, the actual guideline development process requires searching for and critically appraising the current evidence for diagnostic tests. Guideline panel members need to meet face-to-face several times during the process to achieve consensus on various key issues. Firstly, they need to agree on the scope and specific key questions to be addressed in the guideline, including the pre-analytical, analytical, and post-analytical aspects of testing and related candidate biomarker(s). Secondly, panel members need to critically review the best available evidence published in the literature. These may come from analytical and clinical performance studies, randomized controlled clinical trials or meta-analyses that

assess the impact of biomarker-targeted strategies on patient outcomes. Thirdly, members need to review additional literature and formulate recommendations based on the body of evidence and considered judgment of the guideline panel. The process of writing guidelines is expensive and it is essential that all sources of funding and other conflicts of interest are clearly identified so that these factors are not used to disparage the value of the guidelines.

HOW CAN THE ADVICE ON LABORATORY TESTS IN CPGs BE OPTIMISED?

CPGs are usually produced around a clinical scenario in which a laboratory investigation plays only a small, but often critical part within the overall management of that situation. When the CPG writing committee involves no laboratory specialist, the appropriate description of the testing modality and the laboratory issues surrounding it could easily be omitted. Even when the utility of a test is thoroughly evaluated within a clearly defined clinical scenario, there is a risk that the test may then be employed in a different clinical scenario for which the diagnostic utility has not been tested. It is also important to consider whether the guideline provides appropriate methodological information about the actual test recommended, particularly when a test result or clinical decision limit is highly dependent on the assay methodology. The transferability of the evidence from one scenario to the other therefore, must be critically assessed. Arguably this should be to a level of detail above and beyond that required for the clinical aspect, given the test may be used for other purposes.

Laboratory-oriented CPGs often provide detailed and appropriate methodological information on the laboratory tests outlined; e.g. NACB guidance on laboratory testing in diabetes and on tumor markers (8, 9). However, more

commonly, guidelines produced by clinical groups without laboratory professional input, often lack sufficient information. For example in the NICE guidance on chest pain, troponin elevation is discussed, however there is no mention of non-ischaemic causes of a raised troponin, which may be of particular relevance when considering the patient groups in whom troponin is commonly requested. Nor is there any discussion regarding differences between the analytical and clinical performance of assays available on the market (10).

Strategies to improve reporting of analyte-specific laboratory information include a checklist of criteria to consider when interpreting laboratory information in CPGs. A comprehensive list was published in 2012 and suggested 33 pre-analytical, 37 analytical and 10 post-analytical items that should be addressed in a guideline process including laboratory testing (1). Twelve CPGs covering common diseases and conditions were evaluated during the development of the checklist and the mean percentage of topics dealt with by the guidelines was 33%. Information about patient status, biological and analytical interferences and sample handling were scarce in most guidelines even if the inclusion of a laboratory medicine specialist in the guideline production led to increased focus on some typical laboratory related items (e.g., sample type, sample handling and analytical variation).

The checklist has further been used to evaluate the major international CPGs that give advice on using troponins for diagnosing acute coronary syndrome (11). Of the nine CPGs studied, most of the laboratory related checklist items were not considered or needed to be updated. For example, the suggested analytical quality goals were not applicable for the high sensitivity troponin assays and important interferences that may lead to false positive or

negative diagnoses were not commonly mentioned. Recently, another group has appraised the checklist and proposed additional items and modifications (12).

The effectiveness of a CPG needs to be evaluated by assessing the potential improvement in outcome of patients who are managed by the process described in the guideline. This will firstly require an assessment of whether the guidance has been successfully implemented. Secondly, whether its advice has been adhered to and thirdly, that some tangible and measurable quality indicators have been benchmarked against other users of the guideline. It should be recognised that adherence to CPGs is a real issue to be overcome.

WHAT ARE THE BARRIERS TO GUIDELINE IMPLEMENTATION?

How should a laboratory implement a guideline and what are the barriers to implementation? There are many reasons why CPGs are not implemented and this varies with both the condition under scrutiny and the different clinical practitioners. Moreover, since a single CPG can have a number of recommendations, there will be a variation in the overall compliance with the guidelines. Finally, there may be an element of self-deception. In the early days of CPGs, Lomas *et al.* reported that obstetricians were aware of and agreed with CPG recommendations in regards to Cesarean sections but their actual practice did not reflect recommended care (13).

In general, the barriers to implementation can be classified into three domains – knowledge, attitudes and behavior (14). A study of Dutch general practitioners explored the reasons for non-compliance and the key barriers identified were lack of agreement with the recommendations, environmental factors and lack of knowledge of the guidance. The

environmental factors included time pressures, lack of resources, organizational restraints and lack of reimbursements (15). We have recently surveyed laboratory medicine specialists in England regarding two guidelines, one on diabetes and one on chronic kidney disease and found that only 41% and 12% were compliant, respectively (Barth *et al*, unpublished data 2015). Since the barriers of using CPGs in practice can be manifold, it is very important that guideline panels consider these potential issues before they start the actual development process.

HOW DO WE KNOW IF THE GUIDELINE IS EFFECTIVE?

CPGs are written after a distillation of the clinical evidence available for that condition. In the ideal case, the evidence will be of high quality and based on studies examining clinical outcome. However, when there are no outcome data or the evidence is poor, clinical audit of the guideline becomes a means of not only evaluating the adherence and the clinical effectiveness of the CPG, but also providing primary evidence for effectiveness. Meanwhile where guidelines are underpinned by high quality evidence, audit can provide a useful tool for laboratories to assist with demand management, working practices and to aid decision support.

Clinical audit is therefore an essential tool and recommendations for measurable key quality indicators should be included in all CPGs in order to aid the process of monitoring and evaluation of the guidelines' effectiveness. A systematic review suggested that evaluation through audit or other means may improve the effectiveness of the CPG on outcomes overall (16). This would indeed make audit or assessment of guideline effectiveness a

key part of the success of CPGs in changing outcomes.

At present, routine clinical audit to evaluate CPGs following their introduction is not a mandated activity. It is unclear who would be responsible for auditing the diagnostic testing in a CPG. However, since it is well recognized that audits that are not supported by the group being audited have little impact, audits of test usage should be performed by the clinicians ordering the tests. Despite this, laboratories have much to gain by auditing laboratory test utilization and the clinical and cost-effectiveness of testing. In fact, laboratory testing can be used as a surrogate marker of adherence to clinical guidelines e.g. Hb1Ac in diabetes (17), and to support laboratory-level decision making as outlined above.

National schemes for auditing laboratory practices are undertaken in the UK through the activities of the Association for Clinical Biochemistry. These audits have been used successfully to evaluate adherence and practices following CPG introduction (18, 19, 20, 21), however it is not known how many other countries have similar national audit programmes. Clinical Pathology Accreditation (CPA, UK) or other accreditation bodies stipulate the requirement of laboratory practices to be audited regularly (22). Despite the value of this activity in assessing the uptake and wider implementation of best laboratory practice, there is no formal obligation for auditing CPG compliance at present.

CONCLUSIONS

CPGs are widespread and being increasingly produced. Other articles in this journal have focussed on the role of laboratories in synthesizing the evidence-base underpinning guidelines and in ensuring the quality of guideline production. However, the production of a CPG

is merely the first step of a complex process that ultimately puts the best available evidence into daily clinical practice. This process, firstly, involves an evaluation of the laboratory information contained within the CPG to determine if any relevant information is missing. Secondly, attempts should be made to encourage that laboratory professionals are included in CPG development. Thirdly, strategies need to be developed to enhance compliance with national and international CPGs and some form of evaluation, through audit or other means, is developed after the guideline is published and disseminated. The laboratory should rightly be involved in each of these steps, if it is to subscribe to evidence-based best practice.

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