Strengthening methods of diagnostic accuracy studies

Ochodo, Eleanor

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Chapter 9

Systematic reviews of diagnostic test accuracy for evidence-based diagnostic practice in Africa

Eleanor A. Ochodo and Mariska M.G. Leeflang

In 2009, a debate started about whether there was enough evidence to change current guidelines from presumptive malaria treatment of children under five years of age presenting with fever to testing these children before treating them (1,2). A major argument against this policy change was the lack of confidence in the performance of the available rapid diagnostic tests to accurately diagnose malaria in children. This debate nicely illustrates one of the many diagnostic dilemmas’ resource-poor countries are struggling with. It also illustrates the need for more and better evidence about diagnostic questions in these countries.

The ultimate question here may be: should we test before treatment? The ultimate study design would be a randomised controlled trial in which one arm is tested before treatment and the other arm is treated presumptively. However, before such a trial will ever be granted by ethical committees, health care workers, the public or the patients, a little more knowledge needs to be gained on the accuracy and reliability of the available malaria tests. Only when the accuracy of these tests is high enough will policy makers, ethical committees, health care workers and patients put their trust in them. And only when the accuracy of the available tests is known, will it be possible to make a sensible decision about which test one to use in the trials.

The accuracy of a diagnostic test depends on its ability to distinguish people with a target condition from people without the specified condition. A target condition can either be a disease or a specific stage of a disease. Accuracy is often expressed as sensitivity (percentage of people carrying the disease with a positive test result) and specificity (percentage of people who do not carry the disease with a negative test result). Other measures used to express accuracy include the predictive values, likelihood ratios, area under receiver operating characteristic curve and diagnostic odds ratios. In a study evaluating the accuracy of a test, the results of the test under evaluation, the index test is compared to the results of a reference standard. A reference standard is the best available test or method to accurately diagnose a target condition (3,4,5).
In order to assist health care providers, researchers, and policy makers in making rational and evidence-based decisions about the use and interpretation of diagnostic tests, a valid scientific evaluation of the accuracy of tests is required. A valid scientific evaluation can be done by systematically summarising the results of previously published studies. Such a systematic review is a scientific tool that objectively and methodologically identifies, appraises and summarises the existing data from quality primary studies (6). It constitutes the highest level of scientific evidence (7,8). A systematic review may or may not include a meta-analysis, which is a statistical method of summarising results of primary studies into a single and precise estimate (6). The benefits of systematic reviews are substantial. Firstly, they help summarise a large amount of information into a form that can easily be read and used to make decisions. Secondly, systematic reviews establish whether scientific findings are consistent and can be generalised across populations, settings, or whether findings vary significantly according to subgroups. In addition, systematic reviews help to identify the risk of bias in primary studies. The rigorous methods used in systematic reviews limit bias and improve the reliability and accuracy of conclusions. As a result they can effectively assist in guideline development and in translating research into practice (9,10).

Systematic reviews of diagnostic test accuracy in particular are useful in establishing the reasons why the accuracy of tests vary. Test accuracy has been shown to vary with factors such as the patient population, spectrum of disease, disease stage, type of test used, how a test is administered and the expertise of the people administering the test (11). Diagnostic test accuracy reviews are also useful in comparing tests or combinations of tests or different diagnostic strategies (12).

Effective diagnosis in Africa is impeded by limited financial and human capacity, and poor laboratory infrastructure. Poor laboratory infrastructure includes poor assurance mechanisms or a lack of quality assurance mechanisms, a lack of appropriate laboratory reagents and equipment and logistical challenges in specimen collection, storage and transportation. These factors may lead to a lot
of variation or inconsistencies in diagnostic results. Therefore even when laboratory services are available, health workers perceive them as unhelpful and unreliable (13). These variations and inconsistencies are a hindrance to decision making and guideline development. Therefore in this setting, systematic reviews of available studies on diagnostic tests accuracy will be useful in objectively evaluating inconsistencies, and in identifying sources of bias and variation. More so, in a situation where resources are limited, both an accurate diagnosis and the choices made towards that diagnosis are crucial for the optimal use of these resources. The adoption of quality systematic reviews of diagnostic test accuracy will facilitate rational decisions related to which diagnostic tests and resources should be channeled to.

Unfortunately, the capacity to prepare systematic reviews in developing countries is limited by insufficient skills and a lack of access to scientific literature because of a lack of finances to pay for subscriptions to medical journals (14). Access to scientific literature is further hampered by slow internet connections that make it difficult to download articles (15). Concerted efforts are therefore required to promote their use and to build capacity. In its bid to enhance the quality of laboratory practice in Africa the newly established African Society for Laboratory Medicine can help advocate for the use of high standard diagnostic test accuracy reviews to guide evidence-based diagnostic practice (16).

Currently, the most prominent organisation that is actively promoting the preparation and use of systematic reviews is The Cochrane Collaboration (17). Although it is committed to global participation in the use of systematic reviews, The Cochrane Collaboration is still dominated by authors and papers from developed nations. Therefore the evidence from Cochrane reviews may not be applicable to developing countries, which have the largest burden of disease (18).

To address this challenge, the Cochrane Collaboration has embarked on initiatives to actively promote participation from developing countries. These
include building capacity of local authors through the provision of training opportunities, fellowships and by forming partnerships with local institutions. For instance, the Reviews for Africa Programme (RAP) trains and mentors African health researchers to prepare Cochrane Reviews. RAP is a partnership between the South African Cochrane Centre and the Liverpool School of Tropical Medicine. This program focuses on systematic reviews on diseases that are applicable to Africa such as HIV/AIDS, malaria and tuberculosis (19).

To further promote evidence-based practice in Africa, the Collaboration for Evidence Based Health Care in Africa (CEBHA) was recently formed. This organisation is a collaboration between international and local African researchers, its main aim being to facilitate the knowledge and implementation of evidence-based health care in Africa. One of its pillars is to support African scientists to develop systematic reviews through trainings and mentorship. It is currently focusing on Eastern African countries with plans to expand to other African countries in the future (20).

Additionally, in order to enable scientists from developing countries to gain access to scientific literature, the World Health Organization (WHO) in collaboration with major publishers set up the programme, Health Internetwork Access to Research Initiative (HINARI). This programme offers free or low cost access to medical journals for eligible developing countries. This enhanced access to literature can enable African researchers to prepare systematic reviews (21).

Even though Internet connectivity in Africa is still low, it has witnessed a marked improvement in penetration and speed. Latest estimates report an improvement of 2633% in Internet users between the years 2000 and 2011. Broadband initiatives have also been put in place to increase bandwidth, the latest being the availability of fiber-optic cables in some African countries. As Internet access and speed continues to improve, access to scientific literature will also improve (22).
In a nutshell, systematic reviews, when prepared rigorously, objectively summarise the findings from available studies and provide a strong source of evidence. To promote the use of diagnostic test accuracy reviews in Africa, the African Society for Laboratory Medicine can help promote the use of high standard diagnostic test accuracy reviews to guide evidence-based diagnostic practice. Secondly, the importance of these reviews ought to be disseminated to African researchers through workshops and their capacity needs to be built through trainings and mentorship. These can be performed in partnership with the Cochrane Collaboration, CEBHA or other researchers well versed in developing these reviews. Finally, the use of the HINARI programme that was set up to enable researchers from developing countries to access scientific literature needs to be encouraged.

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