Bridging the gaps in evidence based diagnosis

Evidence on diagnostic accuracy and precision is scant and hard to find

Research p 413

The process of diagnosis is complex and poses many challenges to doctors and other clinicians attempting to practise in an evidence based manner. When making a diagnosis in patients who are already ill we should be able to draw on evidence about the accuracy of diagnostic tests. When trying to make an early diagnosis of presymptomatic disease in well people through population screening we rely on evidence from randomised trials on whether patients benefit from such screening. Looking for presymptomatic disease among patients with an unrelated disorder (case finding) or trying to generate a differential diagnosis for patients' signs and symptoms require different types of evidence. We need to match each question to the type of evidence by using a diagnostic strategy.

Furthermore, diagnosis seldom relies on a single test. Ideally a clinician would like to find valid evidence about a cluster of tests, including the clinical examination, along with measures of the accuracy of combinations of these tests. It may also be useful to know how a new test compares with older tests, although this will depend partly on the role of the new test—whether it is a replacement, triage, or add-on test.¹

Reliable evidence about the precision and accuracy of a diagnostic test is hard to find, however, given the recent increase in new laboratory tests and the lack of evidence to support many of them.²⁻⁴ Despite improving standards in research on diagnostic tests in the past decade, the methodological quality of many diagnostic studies remains low.^{w1-w5} Even apparently evidence based sources are flawed—in this week's *BMJ* Mallett and colleagues report that the reliability and relevance of current systematic reviews of diagnostic tests for cancer are compromised by poor reporting and review methods.⁵ This matters because biased estimates of diagnostic accuracy and poorly designed and reported studies can mislead clinical decision making.^{3 w1}

One way to find evidence on test accuracy is the "4S" pyramid approach described by Brian Haynes, which considers evidence resources in turn from systems, synopses, syntheses, and studies (fig).⁶

At the top of the pyramid are systems using explicit review processes to present high quality, pre-appraised evidence. For questions of diagnosis this can be difficult though, because some systems such as *Clinical Evidence* (www.clinicalevidence.com) do not include material on diagnosis, although this is set to change soon. The second tier of the pyramid or search cascade comprises high quality journals of secondary publications—such as *ACP Journal Club* (www.acpjournals.org) and *Evidence Based Medicine* (<http://ebm.bmjournals.com>)—and *bmjupdates* (<http://bmjupdates.mcmaster.ca>), a service that pre-rates primary articles for quality, clinical relevance, and interest. The next tier includes databases of systematic reviews such as the Cochrane Library, but this will not be of much help until the Cochrane Collaboration launches its new process for systematically reviewing evidence on diagnosis. The final tier consists of original studies, which can be identified by using the PubMed clinical queries (www.ncbi.nlm.nih.gov/entrez/query/static/clinical.shtml) diagnosis search filter to search Medline. This search filter has been validated for accuracy,⁷ but not everything relevant to the topic will be found using this approach.⁸ If all else fails a general Medline search might prove useful. However, finding the evidence will provide answers only if the evidence is valid, important, and applicable to the patient in question.^{9 10}

An additional search of the Rational Clinical Examination website (<http://www.sgim.org/clinexam.cfm#RCE>) may answer questions about the accuracy of the clinical examination. This website presents a series of systematic reviews on the precision and accuracy of the clinical examination and provides a search filter for finding relevant articles, although this filter has not yet been validated for accuracy.

All this work to answer diagnostic questions is beyond the scope of most doctors and other practising clinicians. They need evidence that is available quickly in a concise and intelligible form because they cannot spare more than a few seconds per patient to find and assimilate relevant evidence. Indeed, if answers to clinical questions are not found within 90 seconds, searches for evidence are often abandoned.¹¹ Even when

"4S" levels of organisation of evidence from research

evidence is synthesised and packaged, barriers to making evidence based decisions still exist.¹² The creation of meta-search engines that integrate the main evidence resources (through collaboration among the various publishers) could allow effective and efficient searches and facilitate rapid completion of the search cascade.

Evidence based diagnosis needs more primary evidence on diagnosis, more systematic reviews, and appropriate tools to translate the evidence into action. The challenge to clinicians, educators, researchers, funders, journal editors, and publishers is to work together to make this happen. Doctors and other clinicians should demand action now.

Sharon E Straus *associate professor*

(sharon.straus@utoronto.ca)

Department of Medicine, University of Calgary, Calgary AB, T2N 4N1

Competing interests: SES is an associate editor of the journal *EBM* and ACP Journal Club. The BMJ Publishing Group publishes *Clinical Evidence*.

1 Bossuyt PM, Irwig L, Craig J, Glasziou P. Comparative accuracy: assessing new tests against existing diagnostic pathways. *BMJ* 2006;332:1089-92.

- 2 Bates SM, Ginsberg JS, Straus SE, Rekers H, Sackett DL. Criteria for evaluating evidence that lab abnormalities are associated with the development of venous thromboembolism. *CMAJ* 2000;163:1016-21.
 - 3 McAlister FA, Straus SE, Sackett DL on behalf of the CARE-COAD1 Group. Why we need large, simple studies of the clinical examination: the problem and a proposed solution. *Lancet* 1999;354:1721-4.
 - 4 Lijmer JG, Mol BW, Heisterkamp S, Bonsel GJ, Prins MH, van der Meulen JH, et al. Empirical evidence of design-related bias in studies of diagnostic tests. *JAMA* 1999;282:1061-6.
 - 5 Mallett S, Deeks JJ, Halligan S, Hopewell S, Cornelius V, Altman DG. Systematic reviews of diagnostic tests in cancer: review of methods and reporting. *BMJ* 2006;333:413-6.
 - 6 Haynes RB. Of studies, syntheses, synopses, and systems: the "4S" evolution of services for finding current best evidence. *ACP J Club* 2001;134:A11-3.
 - 7 Haynes RB, Wilczynski NC for the Hedges Team. Optimal search strategies for retrieving scientifically strong studies of diagnosis from MEDLINE: analytical survey. *BMJ* 2004;328:1040-4.
 - 8 Lefland MMG, Scholten RJPM, Rutjes AWS, Reitsma JB, Bossuyt PMM. Use of methodological search filters to identify diagnostic accuracy studies can lead to the omission of relevant studies. *J Clin Epidemiol* 2006;59:234-40.
 - 9 Sackett DL, Straus SE. Finding and applying evidence during clinical rounds. The evidence cart. *JAMA* 1998;280:1336-8.
 - 10 Cabana MD, Rand CS, Powe NR, Wu AW, Wilson MH, Abboud PA, et al. Why don't physicians follow clinical practice guidelines? A framework for improvement. *JAMA* 1999;282:1458-65.
 - 11 Straus SE, Richardson WS, Glasziou P, Haynes RB. *Evidence-based medicine: how to practice and teach EBM*. London: Elsevier, 2005.
 - 12 Guyatt G, Rennie D. *Users' guides to the medical literature*. Chicago: American Medical Association, 2001.
- doi 10.1136/bmj.38945.464722.80

Early intervention in acute renal failure

Give intravenous fluids, not loop diuretics

Oliguria and a rise in the plasma urea concentration are normal physiological responses to the haemodynamic changes associated with hypovolaemia, cardiac failure, or sepsis. Clinical decision making during the ensuing hours may determine whether a patient makes a speedy recovery or develops the serious complication of established acute renal failure. This condition still has a mortality of about 50%, despite recent improvements in clinical practice.¹ A meta-analysis in this week's *BMJ* by Ho and Sheridan reviews the evidence on one commonly used and cheap intervention—the loop diuretic furosemide (frusemide)—but finds it to be of little use in preventing or treating acute renal failure.²

Acute renal failure occurs in a variety of different circumstances and can complicate pre-existing chronic renal failure. The traditional split into prerenal, renal, and postrenal causes of acute failure is useful, if only to remind doctors of the need for a systematic approach to diagnosis and management of the underlying cause. It is appropriate that prerenal causes come first, because the treatment of hypovolaemia to maintain renal perfusion is the only reliable means of renal protection,³ and intravenous fluids will probably need to be tried for most patients. This includes elderly patients, in whom comorbidity may complicate the picture, and patients with oedema, who may none the less have depletion of intravascular fluids.

Typically, junior members of the medical staff are responsible for the initial management of these patients. These doctors need early induction into a method of rapid clinical assessment, such as the acute life threatening emergencies: recognition and treatment (ALERT) course.⁴ Doctors should take a

pragmatic and prompt approach to intravenous fluid replacement, based on the patient's blood pressure, capillary refill time, and venous filling. They must watch out for and treat life threatening complications, such as hyperkalaemia, and catheterise the patient to measure the volume of urine hourly.

If the patient remains oliguric after correction of hypovolaemia, the next step is to distinguish between intrinsic renal pathology and obstructive causes. Acute renal failure may be the result of obstruction of the urinary tract, particularly in patients with only one functioning kidney. While total anuria suggests obstruction, the presence of oliguria or even polyuria does not exclude it.⁵

An ultrasound examination of the renal tract is warranted, mainly to identify obstructive changes and also to measure the bipolar length of the kidneys. Small kidneys suggest chronic renal disease. Ultrasound examination can be misleading, however, and additional imaging may be required.⁶ Obstruction should be identified promptly so that it can be treated with urinary catheterisation, ureteric stenting, or nephrostomy. Delay can result in permanent but avoidable renal injury.

The immediate cause of acute renal failure may seem obvious, but contributory factors such as nephrotoxic drugs, metabolic disturbance (including hypercalcaemia, hyperuricaemia, and paraproteinaemia), and occult sepsis should not be overlooked. Epidemics of acute renal failure may follow outbreaks of haemolytic uraemic syndrome associated with diarrhoea, and other infections such as malaria and leptospirosis may cause renal failure by diverse mechanisms.

The more common causes in any location may change over time, as was noted in one unit in the

Research p 420

BMJ 2006;333:406-7