

Defining diagnosis: screening and decision making in primary care

THE phenomenon of somatisation is a touchstone for a number of issues that concern medical practitioners and the patients who seek care from them. It raises important questions about the nature of diagnosis and about the expectation, which both patients and doctors have, of a defined diagnosis. In this issue of the *Journal*, Rosendal *et al* come up against some of these issues in the context of a randomised trial that seeks to improve the diagnosis of somatisation in primary care.¹

The act of diagnosis is a central feature of a doctor-patient interaction. The discipline of arriving at a diagnosis and categorising a problem is what allows medical practitioners to provide predictive information about prognosis and treatment. The certainty that patients may associate with a diagnosis allows them to have confidence that their problem is understood, and provides the basis for the doctor and patient together to arrive at a plan for management. This general approach applies to much of medicine, and particularly to some specialist disciplines in which the process of diagnosis is facilitated by diagnostic tools for refining differential diagnoses into a final diagnosis. But the nature of primary care is different; many presentations are not made specifically for an identified disease,² and consultations may result in a tentative or probable diagnosis with no definitive decision about the underlying nature of the problem. In a primary care setting the first priority is often to exclude serious disease, rather than to make a precise diagnosis of problems that have a high probability of being self-limiting.

The corollary of this is that in the pragmatic world of general practice, lack of certainty doesn't always matter, to the extent that it does not necessarily have an adverse consequence for the health of a patient. The GP's experienced and informed view about what a patient is likely to be suffering from is often enough for the patient and doctor to make the key decisions required of them: whether to reassure, concentrate upon symptomatic relief, investigate further, or refer for specialist opinion. Thus primary care is a setting in which there may be less concern with achieving a precise diagnosis and more concern with making an appropriate management decision.

At one end of the scale of uncertainty in diagnosis we find somatisation. Rosendal *et al* have reported on a randomised trial of a multifaceted training programme, taking the form of small group and didactic training, designed to improve the detection of somatic disorders in primary care. They found that the GPs in the intervention group did not diagnose more somatisation than those who did not receive training. There were no differences between the diagnoses in the control and intervention groups when their agreement with screening questionnaires for somatisation were measured.

The first issue that this study raises is the question of accurate definition. As the authors acknowledge in their conclusion, there is no clear, undisputed, 'gold standard' definition of somatisation. The plethora of terms that may be used to refer to similar phenomena, such as 'somatisation', 'medically unexplained physical symptoms', 'functional somatic symptoms',

'somatoform disorders' or 'psychosomatic illness', merely serve to add to the confusion.³ In this study the authors asked GPs to classify a patient's main problem in one of five categories, ranging from 'physical disease' to 'no physical symptoms', and dichotomised the scale to identify patients with somatisation. This scale makes no distinction between mental health disorders in general, and those that show aspects of somatisation. It implies that patients with mental health disorders should be considered to be somatic, which once again begs the question of how somatisation is defined. The lack of a clear, consistent definition of somatisation is a problem which still bedevils attempts to study the phenomenon.

Beyond the issue of definition, this study raises a more fundamental question about the role of screening tools. In this instance, two screening questionnaires, each with a sensitivity of less than 0.4 compared to a standardised psychiatric interview, are used as a comparison against which to measure diagnosis. Whether this is reasonable must depend to a large extent upon the aim of the diagnostic enterprise that is being evaluated. If the aim is a general one of raising awareness and encouraging GPs to consider somatisation as one of the many possibilities that should be considered in a primary care diagnosis, then a screening tool may be an appropriate benchmark, and a reasonable model against which to compare practice. This is predicated upon the belief that GPs do not pay enough attention to somatisation in the first place, and that screening would represent a qualitative improvement over usual practice. On the other hand, if the aim of the exercise is to measure diagnosis in the more formal sense of accurately classifying a disease, then screening is a less appropriate comparison. Screening is not a synonym for diagnosis; indeed the usual outcome of a positive screening result is an indication that a diagnosis should be confirmed by other means.

A screening tool may be an effective way of identifying patients for further investigation without necessarily relating to a prognosis, or without indicating any given path for patient management. For example, a meta-analysis of studies that trialled routinely administered questionnaires for depression and anxiety, found that applying them as screening tools on a routine basis made no difference to the detection of emotional disorders or difference to patient outcome,⁴ and a recent analysis of screening for excessive alcohol consumption found that applying a screening tool was rarely a precursor for a brief intervention addressing excess alcohol use.⁵ These examples show that it is possible for screening tools to have good sensitivity, but little clinical predictive value. Again, this highlights a challenge for implementing screening in primary care, a setting in which predictive value is central.

Screening, then, is a fundamentally different activity from the task of clinical prediction. Clinical prediction rules, such as the Ottawa ankle rules for ordering X-rays, are clinical tools that quantify the individual contributions that various components of history, examination, and laboratory results make towards diagnosis, prognosis, and likely treatment response of an indi-

vidual patient.⁶ But the proliferation of instruments that have been developed for screening and for clinical prediction leaves open a temptation to confuse the two, and to misapply them in circumstances for which they were not designed. Tools designed to be used for screening are not necessarily effective in cases of individual decision making. This is not to say that there can never be circumstances in which screening tools are appropriate for individual assessment, but the onus must be upon those who wish to use tools in novel ways to justify such use in a systematic fashion.

Rosendal and colleagues address an important issue. Improved diagnosis of somatisation will help clinicians to provide appropriate support and understanding for patients with this disorder. Better diagnosis will help to avoid unnecessary investigations, referrals, and invasive procedures with the attendant problems of cost, delay, and distress for all concerned. The challenge for studies of somatisation that seek to address these important issues is to find definitions of the disorder that can be explicitly related to decisions about therapy, investigation, and referral. Diagnostic categories that can be related to these pragmatic questions will make the greatest difference to patients and clinicians in primary care.

The potential and limitations of personalised medicine in primary care

THE White Paper *Our Inheritance, Our Future* emphasises the government's intention to move molecular genetics into mainstream health care.¹ There are significant implications for primary care, in particular for detection of breast, ovarian and colorectal cancers, prevention of ischaemic heart disease, and screening for antenatal risks. A more surprising implication is the commitment to a personalised medicine approach through the use of pharmacogenetics to tailor prescriptions to the individual.

Pharmacogenetics is the study of the variation in drug responses between individuals due to genetic differences. The subject has existed for several decades with the observation of phenotypes (expressed biological characteristics), such as slow acetylation of some antihypertensives, differential responses to antitubercular drugs, and familial clustering of adverse reactions to anaesthetics.²⁻⁴ Drugs exert their action through receptors and have their blood levels determined by the activity of metabolic enzymes. Receptors and enzymes are proteins, which are coded for by DNA. DNA molecular analysis should therefore reveal patient-specific information about the receptors and enzymes for a given drug, and consequently the effect of that drug at an individual patient level before the patient has taken the drug. The potential benefits are the prediction and avoidance of side effects, prediction of response to treatment and individually tailored advice on lifestyle and disease prevention: the right drug, for the right patient, at the right dose.

This bold statement sounds like unrealistic exaggeration. Indeed, 48% of MEDLINE-cited entries for pharmacogenetics are review articles, with only 11% of articles being original research examining the clinical validity of pharmacogenetic tests.⁵ The technology promises much, but appears to be delivering little. However, there are a small number of papers

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References

1. Rosendal M, Bro F, Fink P, *et al.* General practitioners' diagnosis of somatisation. *Br J Gen Pract* 2003; **53**: 917-922.
2. Starfield B. *Primary care: balancing health needs, services, and technology*. New York: Oxford University Press, 1998.
3. Burton C. Beyond somatisation: a review of the understanding and treatment of medically unexplained physical symptoms (MUPS). *Br J Gen Pract* 2003; **53**: 231-239.
4. Gilbody AM, House AO, Sheldon TA. Routinely administered questionnaire for depression and anxiety: systematic review. *BMJ* 2001; **322**: 406-409.
5. Beich A, Thorsen T, Rollnick S. Screening in brief intervention trials targeting excessive drinkers in general practice: systematic review and meta-analysis. *BMJ* 2003; **327**: 536-540.
6. McGinn T, Guyatt G, Wyer P, *et al.* Clinical prediction rules. In: Guyatt G, Drummond R (eds). *Users' guides to the medical literature: A manual for evidence-based clinical practice*. Chicago: American Medical Association, 2002: 471-85.

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that demonstrate association between pharmacogenetic test results and primary clinical endpoints, and this offers an enticing view of the future. Moving to prospective testing to improve the efficacy and safety of prescriptions is likely to change the consultation fundamentally. For example, DNA is inherited, therefore if an individual is unable to take a given drug then it is likely that some family members will also be unable to do so. The best example of pharmacogenetics in current practice is the use of the thiopurine methyltransferase (TPMT) genotype to guide the prescription of azathioprine, methotrexate and other mercaptopurines in childhood leukaemia, transplants and, potentially, rheumatoid arthritis.⁶ It allows accurate dosing to provide maximum effect with minimal side effects. This, like many other pharmacogenetic genotypes, codes for a single metabolic enzyme. The natural role of such enzymes is to metabolise environmental toxins and carcinogens. Therefore, it is possible that predictive disease associations with cancers may become apparent after a pharmacogenetics test has entered the marketplace.⁷

Test results are probabilistic, not binary; i.e. there is a percentage chance of response and side effects. For example, there is reasonable evidence that possession of a cytochrome P450 (CYP) 2C9 variant allele is associated with an increased risk of major bleeds for those on warfarin (odds ratio = 3.68, 95% confidence interval = 1.43 to 9.50).⁸ What is clear is that not everybody with the variant allele bleeds. Choosing a lower dose of warfarin or avoiding warfarin and taking aspirin instead leads to increased safety at the expense of efficacy. Informed choice regarding such treatment decisions will require the explanation of probabilistic test results to patients and decision rules probably based on health economics.

No health service in the world has ever tried to afford every