A new arrival: evidence about differential diagnosis

You are a primary care physician seeing a 53 year old man who was examined 2 days ago in an emergency department for an episode of syncope. He had been waiting in a long queue when he felt lightheaded and nauseated; then he lost consciousness, with no witnessed seizure activity. He has been healthy, with no known cardiac or neurological disease. In the emergency department, his vital signs and findings on cardiac and neurological examinations had been normal, as were his blood count, blood glucose concentration, and 12 lead electrocardiogram. He was given no diagnosis, and he is now worried about what caused this episode and whether it will recur. Of the many causes of syncope you wonder which should be sought in this patient.

“Differential diagnosis” refers to the methods by which we consider the possible causes of patients’ clinical findings before making final diagnoses. At its heart, differential diagnosis involves acts of selection: we consider a patient’s illness and choose which disorders to pursue further. Is there high quality research that could guide our selections, such as evidence about the frequency of disorders that can cause clinical problems like syncope? If so, wouldn’t it be grand if someone would find it, summarise it, and tell us about it?

The main results of research about differential diagnosis can be expressed as the number and percentages of patients who are found to have each underlying disorder. For instance, in the study by Ammirati et al, of 195 patients presenting with syncope to any of 9 Italian community hospitals, we find that 69 (35%) were diagnosed with neurovascular reflex disorders. From this 35% frequency in the whole sample, we can estimate the disease probability of neurovascular reflex disorders for any 1 patient from the sample to be 0.35 or 35%. In general, conditions diagnosed frequently will have relatively high disease probabilities in the study, whereas those seldom diagnosed will have low disease probabilities.

We can use the study’s disease probabilities as starting points for estimating pretest probability in our own patients and then adjust these probabilities, taking into consideration features of our patients or our practices. For instance, the study by Ammirati et al reports disease probabilities of 35% for neurovascular reflex disorders and 21% for cardiac disorders. The scenario patient’s history (prolonged standing, then premonitory symptoms, then syncope) suggests a neurovascular reflex cause, which raises the pretest probability of a neurovascular reflex disorder for this patient. The absence of cardiac findings on the history, examination, and electrocardiogram lowers the probability of cardiac disorders for this patient.

Once we have them, pretest probabilities can help with diagnostic decisions. Firstly, pretest probabilities can help us to decide whether to pursue specific disorders as explanations for our patient’s illness. A sensible strategy is to choose the most probable disorder as the “working diagnosis” we plan to confirm and then to select from the remaining disorders those few that are likely, serious, and treatable enough to be the “active alternatives” that we plan to exclude. These selections (working diagnosis and active alternatives) form the short list of our initial differential diagnosis, and we would pursue these disorders first. If the short list does not lead us to a diagnosis, we could then consider other disorders with lower probabilities. Secondly, we can use pretest probabilities when choosing which diagnostic tests to use or when interpreting their results. Thirdly, we can also use them when deciding whether to forgo any testing and proceed with treatment.

But why should we bother using evidence for differential diagnosis? Why not rely solely on our clinical experience when estimating pretest probability? Our case memories are as close as our thoughts and are directly calibrated to our practices. But using remembered cases requires us to have had sufficient experience with this problem (dozens or hundreds of cases) and for us to be able to accurately recall this experience. Several biases can distort the frequencies we estimate from remembered cases, as we tend to recall striking or recent individual cases without the proper denominators.

We can’t and shouldn’t stop using remembered cases to estimate pretest probability. Still, it makes sense to know when our memories may be prone to ignorance or bias. For instance, when we’ve had little or no previous experience with a problem or when a newly described clinical problem is reported, we need external evidence to educate our estimates of pretest probability. Alternatively, when we’ve

Beyond these fundamentals, preference will be given to studies that use stronger methods to reduce bias, including prospective designs, explicit diagnostic criteria, and standardised evaluations applied to sufficient numbers of patients. Any clinical problem could qualify, but preference will be given to studies of problems ranging from simple fainting to life threatening arrhythmias.

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particularly the last—keeping up with new research. We hope this
Evidence-Based Medicine
aims to serve all of these needs, particularly the last—keeping up with new research. We hope this new arrival will help you to become better and faster at estimating pretest probabilities and selecting differential diagnoses.

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Journals reviewed for this issue*

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*Approximately 60 additional journals are reviewed. This list is available on request.

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