EDITOR'S CHOICE

Genomics—from the lab to clinical practice

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There are about 20 000 genes in the human genome. Until recently, clinicians seeking to diagnose a genetic condition have had to select single genes to be sequenced. The process is slow, expensive, and often unsuccessful. Now that the cost of DNA sequencing has fallen so dramatically, it's cheaper and easier to sequence the entire genome, with huge potential benefit to our understanding of disease.

But this bounty brings with it clinical and ethical questions, as Caroline Wright and colleagues explain (doi:10.1136/bmj.f6845). Who should be tested? How much of the genome should be sequenced? What should patients be told? What do we do about incidental findings? And how should an individual's genomic data be stored?

Uppermost in clinicians' minds may be the question of how best to interpret the information that is now so abundantly available. It may be easy enough to identify a gene that explains a patient's clinical presentation, such as the genetic variant for Charcot-Marie-Tooth disease. But because of incomplete or age dependent penetrance, finding a genetic variant that is known to cause a disease doesn't mean the person has or will develop that disease. Because we still have limited understanding of many genetic variants, we should beware of overinterpreting the data, say Wright and colleagues. "Our ability to generate data now far outstrips our ability to interpret them."

Sequencing the entire genome will inevitably reveal unexpected findings, some of which will cause confusion and distress. In a linked commentary, Alastair Kent discusses the impact on patients (doi:10.1136/bmj.f6991). The new ease of genomic testing is mainly good news, he says. But the potential for

unexpected findings makes it hard for patients to specify in advance how they would like these to be dealt with. "Do I want to know if my genome reveals that I am likely to develop a serious condition which may or may not be related to the one for which I had DNA analysis in the first place? Is there a difference between diseases that have treatments and those that do not?"

He would like his doctor to discuss these things before proceeding. But what levels of consent need to be obtained ahead of time? Wright and colleagues warn that genomic sequencing too easily becomes screening by another name. As with all screening, we will need to avoid overstating the benefits and underestimating the harms. And each combination of genetic variant and associated disease will need to be evaluated separately in terms of whether the disease is treatable and at what risk and cost.

To stop us straying into untargeted and unmanageable genomic screening, the authors suggest a clinically targeted approach. This would mean partitioning the data and only interrogating those parts that relate to the presenting clinical problem. This would be part of an evidence based policy for genomic testing, which they say is urgently needed. If managed intelligently, with international collaboration and proper education of clinicians, patients, and the public, genome sequencing presents a huge potential bonus to medical practice and research.

Cite this as: *BMJ* 2013;347:f7103

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