

The American College of Medical Genetics is a professional society representing clinical and laboratory geneticists and genetic counselors. ACMG recognizes that genetic testing is playing an increasing role in the delivery of medical care both for rare and common disorders. Genetic tests differ widely in terms of clinical validity and clinical utility. There are some instances, especially in genetic tests for rare disorders, where the clinical validity of a genetic test is obvious – typified by a complete extra chromosome. In other instances, the interpretation of some genetic variants is substantially more challenging. Indeed, in some cases, a particular variant might only be pathogenic in a specific circumstance determined by genetic background or environmental exposure, making it difficult or impossible to ascribe a definitive phenotype to the variant. The challenges are even more complex in studying the genetics of common disorders, where the clinical validity and utility may be less clear, knowledge of genetic contributions to health and disease are far more incomplete, and where the information is likely to be used by practitioners and the public with little experience in working with genetic test data.

The medical genetics community, including clinicians, counselors, and laboratory geneticists, are accustomed to working together to provide up-to-date information on the interpretation of tests related to rare Mendelian and chromosomal disorders. Substantial progress has been made in making genetic tests available for diagnosis of rare disorders and providing expert advice on interpretation of genetic changes that may be unique to an individual. Conducting clinical trials to establish the clinical validity of some of these variants will be daunting and often will be impossible. Any system that requires this level of evidence on clinical validity for genetic test data on rare disorders is more likely to impede than to promote the responsible use of genetic testing in patient care. Imposing a regulatory system on genetic testing for rare Mendelian and chromosomal disorders will likely have serious unintended detrimental consequences. Interpretation of genetic test data for these rare disorders is the core of medical genetics practice and we believe it should be recognized as such.

The genetics of common disorders presents a different set of issues. Here a large-scale population-based approach is necessary, and the potential for misinterpretation and even misuse of data is greater than for rare disorders. There is also less of an existing infrastructure to vet the validity and utility of genetic test data related to multifactorial disorders, and hence a greater need to bring order to the process. If the GTR were to stage its efforts to approach genetic test data, ACMG would suggest beginning here.

Inclusion of information about costs of testing might well be useful for the consumer, but could be a difficult and even misleading form of data to obtain. Testing laboratories often have contracts with specific providers or insurance companies, making it difficult to know the true costs of a test. Cost of testing will also be a moving target in the years to come, converging on whole genome approaches where the cost of interpretation is likely to far exceed the incremental cost of performing a test.

In summary, ACMG suggests that if GTR employs a phased approach that it begin with the genetics of common complex disorders. ACMG is eager to work with its membership and with the larger medical community to integrate new knowledge of genetics and genomics into medical practice. We appreciate this opportunity to comment on the GTR and look forward to working with the NIH to use our experience and expertise to insure that the best quality data on genetic tests are available to the professional and public communities.