primary care providers should offer information to their patients regarding the indications, limitations, risks, and benefits of genetic counseling and testing. They must also be prepared to offer risk-based management following genetic risk assessment. Given the pace of genetics, this is an increasingly difficult task. The field of clinical genetics has rapidly transitioned from single-gene testing to multigene panel testing, with techniques such as whole exome and genome sequencing on the horizon, increasing the complexity of test selection and interpretation, as well as patient education and medical decision-making.

COMMON ADULT-ONSET GENETIC DISORDERS

■ INHERITANCE PATTERNS

Adult-onset hereditary diseases follow multiple patterns of inheritance. Some are autosomal dominant conditions. These include many common cancer susceptibility syndromes such as hereditary breast and ovarian cancer (due to germline *BRCA1* and *BRCA2* pathogenic variants) and Lynch syndrome (caused by germline mutations in the mismatch repair genes *MLH1, MSH2, MSH6*, and *PMS2*). In both of these examples, inherited pathogenic variants are associated with a high penetrance (lifetime risk) of cancer, although penetrance is incomplete (risk is not 100%). In other conditions, although there is autosomal dominant transmission, penetrance is lower, thereby making the disorders more difficult to recognize. For example, germline mutations in *CHEK2* increase the risk of breast cancer but with a moderate lifetime risk in the range of 20–30%, as opposed to 50–70% for mutations in *BRCA1* or *BRCA2*. Other adult-onset hereditary diseases are transmitted in an autosomal recessive fashion where two mutant alleles are necessary to cause full expression of disease. Examples include hemochromatosis and *MUTYH*-associated polyposis. There are more pediatric-onset autosomal recessive disorders, such as lysosomal storage diseases and cystic fibrosis.

The genetic risk for many adult-onset disorders is multifactorial. Risk can be conferred by genetic factors at a number of loci (polygenic), which individually have very small effects (usually with