The need for running matched normal-tumor testing becomes more relevant as one adopts larger gene panels/exome testing. In these instances, matched normal-tumor testing improves accuracy of somatic calls by subtracting germline alterations during bioinformatics analysis. Testing germline samples will identify pathogenic germline alterations in cancer predisposition genes that should be reported to the patient through appropriate genetic counseling. NGS testing is increasingly used in clinical laboratories and does help patients, but there are differences in the complexity of bioinformatics and interpretation of results based on the panel size and the list of specific genes being interrogated. With this complexity, it is imperative that both clinicians and laboratories communicate the pros and cons of different NGS panels and continue to learn from each other using data-driven decision-making tools to continue our mission of helping, not hurting, the cancer patient.

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The Perils of Deprofessionalizing Laboratory Test Ordering: Are We Headed Down a Costly Path?

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Direct-access testing (DAT), in which the patient rather than the physician orders laboratory testing, continues to be a growing market. Demand has been driven by direct-to-consumer marketing, convenience, cost savings, and patient empowerment in managing his or her healthcare. In April 2015, Arizona passed House Bill 2645 (HB2645), which rewrites state law in regard to laboratory testing. HB2645 relaxes regulations related to DAT and allows individuals to (*a*) order any laboratory test without a physician's request or written authorization and (*b*) directly receive test results. The new bill does not require the patient to coordinate with a physician for consultation or interpretation of the results. Furthermore, healthcare providers are not liable for the failure to review or act on a laboratory test result that they did not authorize or order. Finally, HB2645 states that tests do not need to be covered by private insurance or abide by state cost-containment systems.

Those championing these changes argue that DAT will help contain healthcare costs by minimizing the burden on providers, reducing the cost of tests, and empowering individuals to take more interest in their own well-being. However, skeptics are concerned by the limited amount of peer-reviewed studies on the methodologies and performance of DAT and the increasing complexity of tests being offered at a growing number of pharmacies and online retailers. Proponents of HB2645 point out that CLIA regulations do not differentiate between physician-ordered testing and DAT; thus both are performed in CLIA-certified laboratories and must meet the same quality standards. Even so, there are inherent flaws with DAT. Healthcare providers correlate laboratory results with clinical presentation. Even common laboratory tests, such as those used to diagnose thyroid disorders, require interpretation of multiple test results in relation to each other and in conjunction with clinical symptoms.

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As part of a healthcare team, physicians consult with clinical laboratorians when results are not consistent with clinical findings. Furthermore, even experienced physicians are faced with an increasing number of available laboratory tests and the challenges associated with appropriate test utilization, interpretation, and follow-up. Concepts such as pretest probability, positive and negative predictive value, and sensitivity and specificity must be considered when interpreting laboratory results.

CLIA stipulates that reference intervals or normal values must be available to the person responsible for authorizing the test. In the case of DAT, this is the patient. Many normal values are based on population-based reference intervals encompassing the central 95% of the healthy population, meaning that 5% of healthy individuals will have a result outside of the established reference interval. As the number of tests ordered per patient increases, the likelihood of encountering an "abnormal" result increases. It is unclear how individuals will react to results just outside the reference interval. Will primary providers be inundated with requests for consultation? Will emergency departments face a barrage of patients with self-ordered laboratory results? Should the test be repeated at a hospital laboratory, and how will the results compare? If the solution to rising healthcare costs is to promote appropriate test utilization and conserve hospital resources for patients who need them most, it appears that the expansion of DAT may steer us in the wrong direction.

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