COMMENTARY

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The cost of 'free': Advising patients about sponsored genetic testing

In recent years, we have witnessed sponsored genetic testing providing an alternative to out-of-pocket or insurance-billed tests through partnerships between genetic laboratories and biopharmaceutical companies. Available through many laboratories, sponsored genetic testing can be attractive to both patient and clinician in appearing free, but close scrutiny reveals hidden nonfinancial disadvantages that could create ethical challenges for both clinician and patient in our opinion. We break down benefits and drawbacks of sponsored genetic testing for clinicians to use in helping patients make informed decisions.

Sponsored genetic testing must be ordered through a healthcare provider and involves the distribution of genetic data among four possible primary stakeholders: the referring clinician, the patient, a genetic testing laboratory, and a third-party biopharmaceutical or biotech company, with the sponsoring biopharmaceutical or biotech company covering the financial cost. Direct-to-consumer testing is transparent in that it is a consumer-business relationship with costs up front.

ADVANTAGES AND DISADVANTAGES

Sponsored genetic testing is available for many disorders, including epilepsy, skeletal dysplasia, and cardiomyopathies.[1–4] Sponsoring companies may use resulting data to recruit patients for clinical trials, make providers and patients aware of new therapies, or develop new tests for diagnosing genetic diseases.

It may be tempting to conflate sponsored genetic testing with free genetic testing. Our experience has been that sponsored genetic testing is not free. Rather, when patients opt to have their genetic tests paid by the sponsoring company, the laboratory conducts the test and reports the results to the ordering clinician, typically sharing either de-identified or in some cases identifiable results with the sponsoring third party. Data-sharing has significant implications, and being aware of these is important for patient and provider. Currently, there is little guidance for clinicians who are faced with helping patients determine whether sponsored genetic testing is appropriate for them.

In our experience, the benefits of sponsored genetic testing include expanding access to genetic testing and providing opportunity for patients to participate in research. Despite market trends toward lower pricing for out-of-pocket testing and broader insurance coverage, patients seeking genetic testing still face financial barriers.[5] Sponsored genetic testing may be more or equally affordable for patients who could not otherwise access genetic testing, allowing patients access to information regarding disease risks and diagnoses. However, sponsored genetic testing is not the only affordable option. Many laboratories have alternative options for low-cost or no-cost testing that do not involve a third-party sponsor and have financial assistance programs (based on a sliding income-based scale) and laboratory billing policies (such as no balance-billing for those with Medicaid).[6]

Even with the benefits of sponsored genetic testing, clarification regarding potential disadvantages is crucial for addressing practical and ethical issues in best patient care. Ethical issues relevant to clinicians, professional societies, laboratories, and sponsors of sponsored genetic testing involve informed consent and autonomy, confidentiality and privacy, data sharing, equity, assessing clinical appropriateness of breadth of genes tested on sponsored genetic testing panels, access to and clarification of results, and future engagement with laboratory and sponsors.[7–9]

Although professional societies and organizations have published resources regarding many aspects of genetic testing,[10] none address the unique concerns regarding advan-

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tages and disadvantages of sponsored genetic testing.[11] This poses challenges for those lacking familiarity with the nuances of sponsored genetic testing. Laboratories that partner with sponsoring biopharmaceutical companies may promote sponsored genetic testing to healthcare providers, many of whom have limited familiarity with the ethical nuances of genetic testing and counseling, and to patient advocacy organizations for rare diseases through sponsored content and advertisement on public-facing websites (eg, journal articles, Statnews.com). While some sponsored genetic testing offers patients the opportunity to receive sponsored genetic counseling, access to genetic counselors is not guaranteed and varies from program to program. Additionally, the sponsoring laboratories that provide access to genetic counselors and physicians via telehealth may have a financial relationship with the aforementioned sponsors, raising concerns about potential conflicts of interest.

USE OF DATA

One consideration for enhancing transparency around sponsored genetic testing is clarifying how data will be used. Although sponsored genetic testing may not involve payment, when a clinician and patient pursue sponsored genetic testing, both are still engaging in a transactional exchange with the laboratory and sponsoring company. Specifically, patients are exchanging data for the cost of the genetic test. While insurance companies do not have access to results of insurance-paid genetic testing, patients who pursue sponsored genetic testing risk losing control over their data. In other words, one risk of sponsored genetic testing may involve access to de-identified or, in some instances, identifiable data, which are shared with the paying (sponsoring) company.

To date, there are no qualitative studies specifically exploring patient attitudes toward sharing their information with a third-party sponsoring laboratory. Current literature shows that participants have concerns about privacy and confidentiality regarding de-identified genetic biobank research.[12,13] Likewise, a 2018 study[13] on participant views of risks and benefits of general data sharing found that approximately 8% or 61 of 771 expressed serious concerns about access to their data, and less than 8% or 1 in about 12 respondents felt that the potential negative consequences outweighed the benefits. Participant concerns included data theft, data used for marketing, and data sharing decreasing enrollment in clinical trials.[13] Extrapolating from this 2018 study, those with concerns about the risks of data sharing may be in the minority, but their views provide insight that can be used to make data sharing a more transparent process.

In our experience, while some sponsored genetic testing programs provide easy-to-access websites with detailed information on use of data, some programs are unclear about what data will be shared in exchange for sponsored genetic testing. At times, sponsored genetic testing privacy policies can be vague or use legal language that may be obscuring, leading to several questions, such as the following:

- What is meant by de-identified data?
- If sufficient genetic information obtained from a clinical test is shared, is an individual's information then identifiable?
- Could the de-identified data be used for research and development of treatments beyond the targeted genetic test?
- How will data be secured?
- With whom will data be shared (including third parties beyond the laboratory and sponsoring company) and for how long?
- What data will be shared?
- How will data be used?
- Will any data be identifiable?

Additionally, if clinicians order sponsored genetic testing, they should consider the implications for their own practice and for their hospital systems.[14] We have found that while patient data are often (although not always) de-identified, both the laboratory and sponsoring entity may collect the contact information of prescribing healthcare professionals. In turn, per the typical sponsored genetic testing requisitions form, prescribing clinicians may later be asked to recruit patients to participate in a registry or clinical trial. Some laboratories and sponsors offering sponsored genetic testing specify that ordering clinicians and patients are not under obligation to the sponsoring company or laboratory, but others are vague about the relationship between providers and third parties. This consideration may already be part of a clinician's risk-benefit calculation, given prior experience with pharmaceutical companies that use prescribing data for marketing and soliciting patients for clinical trials.

INTERPRETING TEST RESULTS

Concerns about sponsored genetic testing and data also emerge regarding test results that will be shared with the patient.[14] The scope of genes targeted in sponsored genetic testing may reflect the sponsoring company's goals and not necessarily those of the patient and clinician. The broad nature of sponsored

genetic testing panels can be beneficial in many cases, especially when a patient is found to have a medically actionable incidental finding and the ordering provider knows how to interpret the medically actionable findings. Consider, for example, a patient with hypertrophic cardiomyopathy who decides to undergo sponsored genetic testing, which is typically a 30-gene panel. The sponsored genetic testing panel can include genes associated with all forms of hereditary cardiomyopathy or arrhythmia. Instead of finding a variant that caused the hypertrophic cardiomyopathy, the sponsored genetic testing may produce results that lead to a diagnosis of long-QT syndrome, which would otherwise have gone undiagnosed and for which there is a straightforward lifesaving intervention.

Conversely, broader panel testing can result in higher rates of variants of uncertain significance, which are prone to misinterpretation.[14] These results may be considered a benefit or drawback, depending on patient perspective, or may be overwhelming and distressing to patients, especially for individuals who actively wish to not know incidental findings. With broad genetic testing (such as clinical exome or genome sequencing), reporting of secondary findings and patient wishes to have them shared may be presented as an option ("opt in" or "opt out") during the informed consent process.[15] With sponsored genetic testing, secondary findings and opting out of the results of secondary findings may not be an explicit part of the informed consent process.

An example involves a cardiologist intending to test for suspected cardiac transthyretin amyloidosis using sponsored genetic testing with a 100+ gene neuropathy and cardiomyopathy panel that may include testing for autosomal recessive childhood-onset conditions not clinically indicated. Although the testing may return a result that rules out hereditary amyloidosis, the broad nature of sponsored genetic testing may also yield an unexpected result identifying the patient as an adult carrier for an autosomal recessive childhood-onset metabolic condition. While the patient would be informed by the cardiologist that they did not have hereditary amyloidosis, the other findings, including the autosomal recessive childhood-onset metabolic condition, may not be discussed by the cardiologist having not prepared the patient for potential results from the 100+ sponsored genetic testing panel. Without proper counseling, the patient may learn about the unexpected findings (that have an impact on reproductive decision-making) from the results report, which could lead to distress.

When incidental findings are possible and fall outside the scope of the ordering clinician, such clinicians should be prepared not only to facilitate an informed decision prior to testing, but also to ensure the patient has access to adequate posttest counseling. The previous example underscores that access to genetic counseling must occur alongside wide-ranging genetic testing. In making an informed decision to pursue sponsored genetic testing, patients should be made aware of all results a sponsored genetic testing may yield, and a clear plan should be established between provider and patient about how to approach unexpected findings.

GENETIC COUNSELING

Sponsored genetic testing may vary regarding access to genetic counseling. Some programs may offer posttest genetic counseling free of charge, but the service is not standard and may only be available for patients who meet certain criteria. Sponsored genetic testing that offers access to free genetic counseling may eliminate some of the burden on clinicians with little training regarding genetics who have concerns about results that extend beyond their expertise. However, for most sponsored genetic testing, the burden of pretest counseling regarding uncertain or unintended results falls on the clinician. While pretest counseling is an essential duty of the provider, consistent guidance from professional societies and transparency from sponsors of sponsored genetic testing could alleviate some of the burden placed on providers.

INFORMED CONSENT

Currently, there is no standard informed-consent process for sponsored genetic testing, and the level of information varies across sponsored genetic testing offerings. Often it seems that sponsored genetic testing involves a blanket consent that centers on the rights of the laboratory to disclose information to third parties. The third parties are not always clearly defined, nor is it clear how third parties are vetted by the laboratory. In some ways, the flow of data resulting from sponsored genetic testing is similar to a biobank, but with less transparency about what qualifies a third party to become a sponsor (other than financial capability).[16,17] A defined informed-consent process, beyond a company-provided website, brochure, or form, may help clinicians meet the clinical obligation to each patient's unique medical needs. Without a disclosure statement describing potential future uses, patients do not know whether a company can sell their data to

other companies, or what happens to data if companies become insolvent. Existing academic literature on informed consent and data sharing can provide useful guidance for developing an informed-consent process for sponsored genetic testing.[18–20]

General healthcare providers as well as patients need better educational resources provided by relatively neutral experts to complement the informed-consent process. Additional resources to support informed decision-making by patients should be generated by medical institutions, professional societies, or trusted sources like the US Centers for Disease Control and Prevention and the National Institutes of Health, and made available on their respective websites. Such resources may take the form of frequently asked questions (FAQs) on webpages addressing the basics of sponsored genetic testing that providers can use to facilitate conversations with their patients. Handouts with sponsored genetic testing provider FAQs and patient FAQs are available in the online version of this article.

THE BOTTOM LINE

Many of these issues will resonate previous debates about data, biobanking, electronic health records, and commercial genetic testing.[21,22] Although sponsored genetic testing may help enhance access to genetic testing for many and provide researchers with data to develop new therapies, a lack of resources about the disadvantages of sponsored genetic testing for patients and providers who do not specialize in genetics poses challenges for informed use. In lieu of position statements or policy statements from specialty societies and other organizations, we offer these statements for consideration to help practitioners who may be interested in ordering sponsored genetic testing for their patients.

DISCLOSURES

Dr. Ford reports serving as advisor or review panel participant and teaching and speaking for Neuropace. The other authors report no relevant financial relationships which, in the context of their contributions, could be perceived as a potential conflict of interest.

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