Uncertainty Over DAT Testing

By Charlie Schmidt

Dr. Kimberly Lovett was frustrated. Her patient had tested positive on the fecal occult blood test used in colon cancer screening, and as a primary-care doctor in the Department of Family and Preventive Medicine at the University of California, San Diego, Lovett knew the next step in confirming the diagnosis was a colonoscopy. “But why can’t you order the blood test?” demanded her patient, determined to avoid colonoscopy at all costs. Lovett responded that such a test doesn’t exist, yet the patient was adamant that it did—he claimed to have seen it advertised by a Web-based company that sells blood biomarker analyses. After a tense conversation, Lovett’s patient was convinced that the ad had misled him, but he left bewildered, wondering why a company can claim it can diagnose colon cancer when it can’t.

Many practicing physicians wonder the same thing. Direct-access testing (DAT) companies that sell blood screening capabilities to the public are becoming more widespread. These companies, which solicit orders online and then farm the analyses out to large commercial laboratories, charge far less than what doctors ordinarily charge for biomarker testing. Those who work for the DAT industry claim that their services empower patients and allow individuals to get bloodwork done without involving insurance companies, which might raise rates or drop coverage depending on results. But clinicians like Lovett also know that cancer biomarkers in particular have limited utility at best, and then only in the context of other, patient-specific data. “There’s a lot of misinformation out there,” Lovett says. “The danger is that patients might trust the tests more than they trust their own doctors.”

Most DAT companies hire physicians or nurses who review online orders and then supply requisite paperwork to the testing laboratory closest to the ordering customer. Two commercial laboratories (which also work for hospitals, universities, and many other businesses) account for almost all DAT testing in the U.S.: LabCorp in Burlington, N.C., and Quest Diagnostics in Madison, Wis. With 1,400 domestic facilities, LabCorp accounts for the largest share of the DAT business, according to Bruce Friedman, M.D., a retired pathologist from the University of Michigan, who now runs a blog called Labsoft News. Analytical results typically go back to the DAT company, which then communicates with the customer who placed the order.

Surge in DAT

Public data on DAT’s growth aren’t available, and LabCorp’s spokesperson, Stephen Anderson, declined to answer specific questions about the company’s involvement in the business. His sole comment, delivered by e-mail, was that DAT should be performed only if ordered by an authorized provider licensed in the state where the patient lives.

Online orders have propelled dramatic growth in DAT. Through a rudimentary Google search, described in an editorial published last May in the Journal of Clinical Oncology, Lovett identified eight such companies. One of them is Health Testing Centers, which has long offered DAT services to the public from its physical location in Oakland Park, Fla. The company’s president, David Lovely, says online purchases drew in a national customer base that now accounts for 90% of company sales. Moreover, during the last 5 years, those purchases doubled the company’s annual revenues to more than $1 million.

The biggest sellers, Lovely says, include complete blood counts, metabolic panels, and lipid profiles. Cancer biomarkers account for less than 10% of sales, he adds, the most popular being prostate-specific antigen. But Health Testing Centers also sells CA-125—advertised as the “premier test for the diagnosis and management of ovarian cancer,” for $79; CA-19-9, a “powerful tool for the detection of pancreatic or gastrointestinal cancer,” for $129; and other cancer biomarkers, including, but not limited to, CA 27.29, carcinoembryonic antigen, and alpha-fetoprotein. Like other DAT companies, Health Testing Centers also sells a pair of sex-specific cancer screening panels, which include the tumor biomarkers described above, in addition to a collection of “basic health screening” indicators for $499. “Our clinicians use their own judgment about when to proactively call a patient to describe what the results mean,” Lovely says. “We want to make sure patients know that if they get a bad result, they need to see a doctor.” As to the viability of the cancer tests themselves, Lovely responded, “We are loath to get involved in that conversation. We don’t make judgments about whether someone should or should not get a test; we just provide access to it.”

None of the other seven companies identified in Lovett’s editorial (which does not represent a comprehensive list of DAT firms in business today, she emphasizes) offers any form of follow-up for test results. “And none of the biomarkers they sell is specific to the type of cancer they purport to screen for,” she adds. A key problem, Lovett says, is that the tests often generate false-positive results that lead to unnecessary care. Still, Lovett adds, given heavily publicized concerns over health care rationing, patients tend to trust their own
**Regulatory Arena**

Federal regulators have limited jurisdiction over the DAT industry, according to Liz Mansfield, Ph.D., director of personalized medicine in the Office of In Vitro Diagnostics at the U.S. Food and Drug Administration. The FDA restricts its oversight to the accuracy of the test method and the clinical quality of the biomarkers themselves, Mansfield says. After that, whether to allow DAT is a question for the states. According to Friedman, roughly half the states allow DAT without any limitations. “A complete list is hard to generate because of state-by-state variations in the types of biomarkers allowed,” Friedman says. “But the number of states that do allow DAT appears to be increasing, because of a trend among lawmakers to empower patients in ways that allow them to take more control over their care.” (Friedman says he receives no funding from the DAT industry but adds that laboratory advertising supports his blog.)

Madeleine Biondolillo, director of the Bureau of Health Care Safety and Quality at the Massachusetts Department of Public Health, says four states ban DAT outright: Massachusetts, New York, New Jersey, and Rhode Island. But that number reveals an increasingly favorable landscape for DAT, which 18 states banned in 2001, according to a paper published that year in *Laboratory Medicine* by Matthew Schulze, then a senior manager with the American Society of Clinical Pathology in Washington, D.C.

Two recently published papers on mammography for women in their 40s could herald a new era of risk-based cancer screening. But though the idea of targeting screening tests at those most likely to benefit is attractive on many levels, experts caution that much work remains to be done before widespread implementation.

According to the two complementary papers, published in the *Annals of Internal Medicine*, the benefits of biennial mammography screening outweigh the potential harms for women aged 40–49 years who are at increased risk of breast cancer. The analyses found that a 40-something woman with twice the average risk has the same harm-to-benefit ratio as an average-risk woman older than 50 years. Either of two risk factors could double a woman’s risk: having a first-degree relative with breast cancer or having very high breast density.

Of the nearly 230,000 U.S. women who will be diagnosed with invasive breast cancer this year (according to estimates of the American Cancer Society), approximately 39,000 will be in their 40s. The new findings apply to just over 20% of them: 9% of women aged 40–49 have a first-degree relative with breast cancer, and 13% have extremely dense breasts.

The first paper, by Nicolien van Ravesteyn, M.Sc., of Erasmus Medical Center in Rotterdam, the Netherlands, and colleagues from the Cancer Intervention and Surveillance Modeling Network (CISNET), was a comparative modeling study. Its objective was to determine the relative risk at which the harm–benefit ratio of screening women in their 40s equals that of women older than 50. (For harms, the CISNET investigators focused on false-positive mammography results, the most common and most easily quantifiable of the potential downsides of screening. For benefits, they looked at life-years gained and breast cancer deaths averted.)

The second paper, by Heidi Nelson, M.D., of Oregon Health and Science University, and colleagues, was a meta-analysis aimed at defining and validating the personal factors associated with increased breast cancer risk.

For women aged 40–49 years, having extremely dense breasts (category 4 in the Breast Imaging Reporting and Data System, or BI-RADS) or a first-degree relative with breast cancer increased their odds of getting the disease at least twofold. A previous breast biopsy, a second-degree relative with breast cancer, or heterogeneously dense breasts (BI-RADS category 3) increased their risk by a factor of 1.5–2.

A few factors were associated with lower-than-average risk, including body mass index of 25 or higher in premenopausal women, low breast density, menarche at age 15 or older, breast-feeding, and estrogen-only hormone therapy. However, the magnitude was smaller.

“Our research suggests the benefit–harm balance is tipped in favor of every-other-year screening for women in their 40s who are at about twice the average risk of developing breast cancer,” said Jeanne Mandelblatt, M.D., associate director for population sciences...