

Perspectives

Direct-to-consumer genetic testing: good, bad or benign?

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A wide variety of genetic tests are now being marketed and sold in direct-to-consumer (DTC) commercial transactions. However, risk information revealed through many DTC testing services, especially those based on emerging genome wide-association studies, has limited predictive value for consumers. Some commentators contend that tests are being marketed prematurely, while others support rapid translation of genetic research findings to the marketplace. The potential harms and benefits of DTC access to genetic testing are not yet well understood, but some large-scale studies have recently been launched to examine how consumers understand and use genetic risk information. Greater consumer access to genetic tests creates a need for continuing education for health care professionals so they can respond to patients' inquiries about the benefits, risks and limitations of DTC services. Governmental bodies in many jurisdictions are considering options for regulating practices of DTC genetic testing companies, particularly to govern quality of commercial genetic tests and ensure fair and truthful advertising. Intersectoral initiatives involving government regulators, professional bodies and industry are important to facilitate development of standards to govern this rapidly developing area of personalized genomic commerce.

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Over the past few years direct-to-consumer (DTC) genetic testing has received a great deal of attention. In 2008, *Time* magazine selected the genetic test kit sold by the company, 23andMe, as retail invention of the year and the entire area continues to garner significant media attention, both positive and negative. While data on public interest are just starting to emerge (1), there are reasons to believe (via blogs, news media, and anecdotal reports) that consumers are accessing these services for a variety of reasons, ranging from pure curiosity to the exploration of disease predispositions. What does this trend mean for Canadian consumers, physicians and public health insurance programs? What are the issues and how should they be addressed?

A new era?

The DTC genetic testing phenomenon is the result of a rapid evolution in testing technology. Most Canadian physicians are familiar with ordering diagnostic genetic tests for their patients. These tests, which are usually covered by our health care system, detect mutations that are either diagnostic or reasonably predictive and the tests have normally been subject to at least some analysis prior to their implementation.

But DTC testing presents a new paradigm. First, many of the tests advertised and sold via the Internet have not undergone clinical evaluation. The tests can jump straight from the pages of the science journals to the slate of services offered by

testing companies. Second, the tests can be ordered directly, without having to visit a healthcare professional and thus are interpreted on their own instead of being just one part of a comprehensive clinical and laboratory workup. Third, and perhaps most importantly, the health value and personal ramifications (both good and bad) of the tests remain unclear.

Indeed, the tests fall on a broad continuum (see Box 1), with some ostensibly offering little more than a genetic curiosity (e.g. a gene variant that determines ear wax characteristics) to those that relate to cancer predisposition. With a vial of spit and a postage stamp, consumers can acquire information about how their personal genetic makeup affects their susceptibility to conditions like cancer, cardiovascular disease and diabetes. They can also learn about genetic factors that may influence their body’s reaction to certain foods, alcohol, drugs and caffeine, as well as genes associated with eye color, male pattern baldness, and athletic performance.

DTC genetic tests have been widely criticized and their health value questioned. A *Lancet Oncology* editorial called DTC tests for cancer and other conditions ‘flawed and unethical’ (2) and the American Society of Human Genetics cautions that ‘consumers are at risk of harm from DTC testing’ because of inadequate regulatory oversight (3). A recent study of published meta-analyses and HuGENet (Human Genome Epidemiology Network) reviews of gene–disease associations relevant to DTC genetic tests for common diseases concluded that the ‘scientific evidence for most associations between genetic variants and disease risk is insufficient to support useful applications’ (4). The authors suggest ‘it could take years,

if not decades, before lifestyle and medical interventions can be responsibly and effectively tailored to individual genomic profiles’ (4).

In part, this is because the vast majority of variants covered by DTC genetic tests are of extremely low predictive value (5). In addition, many of the health care benefits attributed to these tests require the individuals to use the genetic predisposition information to inform healthy lifestyle changes, most of which they probably should do regardless of the test outcome. To make matters worse, available evidence suggests that it is very difficult to get individuals to make sustained, behavioral changes, even in response to genetic information (6). Several US research groups have recently launched large-scale studies to investigate the impact of genetic information on risk perception and behavior change (see Box 2).

A social issue?

Given the low predictive ability and questionable health value or impact of many DTC genetic tests, why should they be of policy concern? Although they may have limited value (a conclusion that is, admittedly, hardly definitive), could they still pose a threat to consumers? Possibly.

Testing could lead to increased costs for healthcare systems. A recent Internet based survey by McGuire et al. in the United States (*n* = 1087) found that 78% of those individuals who considered using genetic testing services would ask their physician for help interpreting test results (1). In other words, despite the still questionable utility of these tests, patients will likely take results to their physicians, thus increasing the pressure on an already overburdened healthcare system.

<p>Box 1. Tests offered by five or more DTC genetic testing companies that claim to provide genetic risk information Number of companies offering the service is noted in brackets (Source: Genetics and Public Policy Center, 2009)</p>	
<p>Personal genome service (genomic profiling package for numerous conditions) [8] Addiction [5] Alzheimer disease [8] Arthritis [6] Asthma [5] Athletic performance (genes that influence) [7] Cancer (e.g. breast, colorectal, lung, ovarian, prostate, stomach) [10] Cardiovascular disease [16] Celiac disease [8]</p>	<p>Drug response (pharmacogenetic testing) [8] Fetal gender [5] Gastrointestinal disease [8] General nutrition (nutrigenomic testing) [8] Glaucoma/age-related macular degeneration [6] Hemochromatosis [7] Multiple sclerosis [5] Osteoporosis/bone health [10] Recurrent pregnancy loss [5] Restless leg syndrome [5]</p>

Box 2. Genetic information, risk perception and behavior
Investigating the impact of genetic information on behavior
Key studies in progress in the United States

Corriell Personalized Medicine Collaborative

- This non-profit medical research group is offering free genetic testing to an anticipated 10,000 volunteers. Participants will receive test results and advice about lifestyle modifications to reduce disease risks. See: www.coriell.org/index.php/content/view/92/167/

Navigenics and Mayo Clinic Collaboration

- Navigenics is co-sponsoring clinical trials with researchers at the Mayo Clinic to investigate psychological and behavior reactions to different sources of risk information (e.g. genetic test results, family history). Information will be presented with or without counseling to study impacts of different risk communication strategies. See: www.navigenics.com/about/pressreleases/release/040808-genome-analysis-research-trial/

Scripps/Navigenics/Affymetrix/Microsoft Collaboration

- This study will offer genetic scans to up to 10,000 employees, family members and friends of the non-profit Scripps Health system in San Diego and will assess changes in participants' behaviors over a 20-year period. Affymetrix will conduct genetic analyses and results will be available through Navigenics. Individuals can store and access their health information in a Microsoft HealthVault account. Tests are for 20 health conditions that may be influenced by lifestyle, including diabetes, obesity, cardiovascular disease (CVD), and some forms of cancer. See: <http://www.navigenics.com/partners/scripps/>

deCODE Genetics and Duke University Collaboration

- Beginning March 2009, 1000 participants will be recruited to 'assess the clinical utility of a genetic test for type 2 diabetes risk in combination with standardized risk assessment compared with standardized risk assessment alone, and to measure whether changes in perceived risk following genetic testing for type 2 diabetes risk are correlated with behavior change and increased concern about risk for type 2 diabetes'. See: <http://clinicaltrials.gov/show/NCT00849563>

National Human Genome Research Institute (NHGRI)

- The NHGRI has launched a Social and Behavioral Research Branch to 'investigate social and behavioral factors that facilitate the translation of genomic discoveries for health promotion, disease prevention, and health care improvements. This research encompasses four conceptual domains: (1) testing the effectiveness of strategies for communicating information about genetic risks; (2) developing and evaluating behavioral interventions; (3) using genomic discoveries in clinical practice; and (4) understanding the social, ethical, and policy implications of genomic research'. See: www.genome.gov/11508935

The DTC genetic testing industry defends DTC testing by arguing that an individual's genetic information is theirs to know and suggest they do not make medical diagnoses, but rather are 'enabling consumer access to research knowledge' (7). But the McGuire study found that

consumers' primary reason for accessing these services was to gain health information and to assist in medical care.

There is also speculation that DTC testing will generate undue stress and the 'worried well', that is, individuals who over-interpret, and worry

Box 3. Communicating ‘risk’

Most people understand that the term ‘risk’ refers to the probability that an event will happen. In the DTC realm, risk (or the less value laden: chance) typically refers to the positive predictive value or the probability that an individual with a positive test result has or will go on to develop the trait/condition. For example, if one tests positive for the Huntington’s gene, it is certain that the individual will develop the disease. A positive test for the BRCA mutations means that an individual has, roughly, a 50–85% of developing breast or ovarian cancer in their lifetime. But most of the variants that are tested for by DTC companies are of much lower predictive value. For example a positive test for heart disease means that an individual’s risk of having a heart attack by the age of 65 increases from 1 in 100 to about 2 in 100. The clinical value of this kind of genetic test is less than the clinical value of measuring weight, blood pressure and/or cholesterol. Communicating about risk should ideally lead to better understanding and decision making. There are, however, a number of challenges that may confound this goal. Many individuals (perhaps aside from adept gamblers and numerate others) don’t fully comprehend that these representations of risks represent estimates and re-interpret them based on their own personal experiences. Moreover, the language (e.g. quantitative vs qualitative terminology, framing of risks to include converse risk) and presentation style (e.g. odds ratios vs relative risks, rates vs proportions, use of visual aids, etc.) of the communicator may significantly influence comprehension and contextualization.

about, the significance of a genetic predisposition. There is actually little evidence from clinical studies that, for most people, learning of an increased genetic risk for disease leads to ongoing adverse emotional impacts (as found in a 2008 systematic review of 65 studies examining emotional and behavioral impacts of genetic testing) (8). However, what is not clear is whether pre-test counseling (not available for many DTC tests) prevents the most emotionally vulnerable, that is, individuals that evidence shows may become overly anxious (8), from proceeding with testing, or for agreeing to testing because of perceived benefits to relatives rather than to the individual. Finally, some people overestimate the value of gene variants that lower disease susceptibility (‘protective’ variants), potentially leading to reduction in healthy, preventative behaviors.

Next steps?

Given the still uncertain nature of both the harms and benefits, what should and can be done? Internationally, regulatory approaches to DTC genetic testing vary widely. A few European countries and US states permit access to genetic tests only through health care professionals, but many other jurisdictions have no or few regulatory controls specifically related to DTC tests and services (9). Some laws that regulate medical devices, such as the Canadian *Food and Drugs Act* and the US *Clinical Laboratory Improvement Amendments*, do not clearly apply in the context of DTC genetic tests. As such, the current

formal regulatory options for the oversight of validity and utility are relatively limited. As DTC testing becomes more common and a clearer understanding of harms and benefits emerges, new regulatory options may need to be explored.

Meantime, health care providers, particularly family physicians, need to be equipped with the skills necessary to answer questions about the risks, benefits and limitations of DTC testing. This is a new role for most physicians and represents a significant challenge. More broadly, we need to develop new ways of communicating and explaining risk, a notoriously tricky concept that lies at the heart of many of the issues associated with DTC testing (see Box 3).

Finally, steps should be taken to ensure that the information being disseminated is as accurate and understandable as possible. Industry and government representatives in the United States and United Kingdom are working to develop voluntary codes of responsible business practices for DTC genetic tests (9). This is a positive step that should be encouraged; at a minimum, there should be industry standards regarding acceptable advertising claims for DTC genetic tests (10).

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