DIRECT TO CONSUMER GENETIC TESTING

Bottom line: Direct-to-consumer genetic testing (DTC-GT) is over-the-counter genetic testing available online to consumers through private companies. Generally, results report an individual's risk to develop a medical condition as being below average/low, average/general population, and above average/ high based on genome wide association studies (GWAS). Results may provide medically useful information for consumers and potentially provide support and motivation for lifestyle changes (e.g. weight loss, smoking cessation) or even more vigilant surveillance (e.g. breast cancer screening), reveal carrier status of single gene conditions (e.g. cystic fibrosis), effectiveness and side-effect risk of certain pharmaceuticals, in addition to medically irrelevant information (e.g. curly hair). Currently, DTC-GT is not regulated or accountable to an appropriate governing body. Numerous professional societies express concern about how DTC-GT is marketed to consumers, what and how information is provided and the lack of genetic counselling. **Family health history-based risk assessment is still the gold standard in initial assessment for heritable conditions.**

WHAT IS DIRECT –TO-CONSUMER GENETIC TESTING?

Direct-to-consumer genetic testing (DTC-GT), also referred to as personal genome testing, refers to genetic testing available for over-the-counter purchase without the requirement of health care provider involvement. Generally, DTC-GT is marketed with the promise of providing predictive genetic risk assessment for a variety of health conditions (e.g. diabetes, cancer, obesity) and information regarding response to and/or side-effect risk of certain pharmaceuticals (e.g. clopidogrel, statins). Increasingly personal genome testing companies are requiring provider involvement.

DTC-GT uses data generated from genome-wide association studies (GWAS). GWAS are case-control studies which examine many common variations in our genetic code (single nucleotide polymorphisms [SNPs]). They compare large groups of individuals (unaffected controls versus individuals with symptoms of a specific disease or those experiencing a particular medication response) in an attempt to distinguish between non-harmful changes in the DNA code and pathogenic, disease causing/predisposing changes. SNPs (pronounced 'snips') are the most common type of genetic variation. Each SNP represents a difference in a single DNA building block, a nucleotide. SNPs occur normally in an individual's genome about once in every 300 nucleotides, thus there are about 10 million SNPs in the human genome.

DTC-GT uses odds ratios and relative risks to categorize an individual as at increased risk (higher than average), average (general population risk), or at decreased risk (lower than average).

DTC-GT can also screen for single gene disorders (e.g. cystic fibrosis, *HFE*-associated hemochromatosis). Additionally, DTC-GT is advertised to assist in diet and exercise planning and can uncover medically irrelevant information such as bitter taste perception or curly hair.

Generally, DTC-GT is available online to anyone for a cost. Genetic testing for DTC-GT is usually performed on a saliva sample.

Appropriate pre- and post-test counselling is rarely offered by the DTC-GT company or accessed by consumers when available. Ideally, it should be carried out so that the consumer is informed of what the results might reveal (e.g. risk of multifactorial conditions that arise due to the combined contribution of genetic and environmental factors, carrier status of single gene conditions, including cancer predisposition syndromes) and the potential for results requiring additional medical follow-up not limited to behavioural modifications (e.g. vigilant breast screening and discussion of prophylactic surgery as a result of a *BRCA* gene mutation). The implications for extended family members should be addressed. Pre- and post-test genetic counselling has been demonstrated to aid in countering patient distress and encouraging patients to be proactive in their use of test results.

WHAT DOES THE GENETIC TEST RESULT MEAN?

While there are limited data to support the clinical validity (ability to predict clinical outcome) and utility (the likelihood of improving patient outcome), some consumers might benefit from DTC-GT as results may:

- Encourage positive behaviour modifications (e.g. increase exercise, smoking cessation)
  - Although, a recent longitudinal study demonstrated no differences between baseline and follow-up in consumer's dietary fat intake and exercise behaviour in response to DTC-GT results
- Provide useful information for medication choice, dose or management
- Provide information to individuals who have no or limited information about their family history (e.g. an individual who was adopted)
- Reveal carrier status of a genetic condition that could have implications for family planning

Caution when interpreting DTC-GT should be exercised as:

- DTC-GT does not take into account numerous factors important when interpreting genetic test results such as age, family history, lifestyle (e.g. smoking, obesity) and other environmental factors that are a significant contribution to common complex disease development
- **Family health history-based risk assessment is still the gold standard in the initial assessment for heritable conditions**

The impact on a publicly funded health care system of the result of a privately obtained test that suggests additional follow-up (e.g. blood tests, colonoscopy) which is not otherwise indicated is unclear. There are limited prospective studies with actual DTC-GT consumers and longitudinal follow-up. Referral to a specialist or confirmation of test results in a clinical laboratory may be indicated in some circumstances to clarify appropriate surveillance and management.

Additionally, "misattributed equivalence" is a great concern associated with personalised genome testing. There is a fear that if a DTC-GT test were to indicate a lower than average lifetime risk for a certain condition, when family history indicated a much higher risk, a consumer could be falsely reassured and not be as vigilant about medical interventions indicated by family history. This phenomenon speaks to the need for knowledgeable health care provider involvement in pre- and post-test counselling. On the other hand, recognizing the limitation of self-reported family history (incorrect or incomplete information), there may be potential for DTC-GT to add to risk interpretation in some situations (e.g. response to and/or side effect risk of certain pharmaceuticals).

In Canada diagnostic laboratories are provincially regulated. At the time of writing, no DTC-GT is operating under approved provincial regulation, although some may meet USA federal standards (e.g. Clinical Laboratory Improvement Amendments, CLIA). Companies that are not regulated could have staff performance, test analysis and interpretation of results that may not be certified or licenced by any appropriate governing body.

Additionally, privacy is a major concern. DTC-GT companies have self-imposed policies that claim a consumer's genetic information will not be shared, although there is no regulation to dictate what happens if/when a company is sold or goes out of business. Patients should be advised to look into the privacy policy prior to purchasing DTC-GT.

RESOURCES

See www.geneticseducation.ca for more details and how to connect to your local genetics centre. To learn more about Canadian ethnicity-based carrier screening recommendations see the point of care tool

For a recent review on DTC-GT see Scott Roberts *et al*. Direct-to-Consumer genetic testing and personal genomics services: a review of recent empirical studies. *Curr Genet Med Rep.* 2013; 1(3): 182–200

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