

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 medications, 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?^{1,2}

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 complex health conditions (e.g. diabetes, cancer, obesity) and information regarding response to and/or side-effect risk of certain medications (e.g. clopidogrel, statins). Additionally, DTC-GT is advertised as assistance in diet and exercise planning. Testing can uncover medically irrelevant information such as bitter taste perception or curly hair.

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

WHAT DO THE GENETIC TEST RESULTS MEAN?

Test results for DTC-GT depend on what condition is being tested and what technology is being used.

Appropriate pre- and post-test counselling are rarely offered directly by the DTC-GT company and are inconsistently accessed by consumers when available³⁻⁶. Ideally, testing should be carried out so that the consumer knows 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 understands the potential for results requiring additional medical follow-up, not limited to behavioural modifications (e.g. vigilant breast screening and discussion of risk reducing surgery as a result of a *BRCA* gene mutation). The implications for extended family members should be addressed.

Multifactorial disorders and 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.

Odds ratios and relative risks are used to categorize an individual as at increased risk (higher than average), average (general population risk), or decreased risk (lower than average). Results from GWAS may be used to report an individual's risk for cancer, heart disease or diabetes. Test laboratories use variable literature sources, data set and technologies for testing and variant classification which adds complexity to interpretation.

Mendelian disorders and ethnicity-specific testing or next generation sequencing: Single gene disorders (e.g. cystic fibrosis, *HFE*-associated hemochromatosis, *BRCA*-associated hereditary breast and ovarian cancer syndrome) are often screened for by targeting only ethnicity-based gene variations. For example, screening for mutations in the *BRCA1* and *BRCA2* genes is limited to the three commonly found in individuals of Ashkenazi Jewish ethnicity, regardless of the consumer's reported ethnicity. This means that not all clinically relevant mutations or even

genes are necessarily included in analysis; possibly resulting in false reassurance with negative results⁷. This is of particular importance where there is a known family history.

Additionally next generation sequencing (NGS) may be employed, where the entire coding region of a gene is sequenced (read) looking for significant variation as compared to a reference sequence. While some variations are well known to be either pathogenic or benign, some require expert analysis by a genomic specialist. Genetic changes that are only weakly associated with disease may be reported, possibly leading to anxiety or inappropriate additional testing⁷. Additionally, due to variability in interpretation, there is the possibility of conflicting risk interpretations between companies.

Pharmacogenomics: The goal of pharmacogenomics is to identify gene-drug interactions to improve the safety and efficacy of medications⁸. Currently, few DTC-GT companies offer pharmacogenomics as part of their testing menu. Like genetic testing for Mendelian disorders, pharmacogenomics testing is highly dependent upon ethnicity-based gene variations⁸. Most often companies are analysing for specific SNPs in genes that code for enzymes key to specific drug/drug class metabolism e.g. CYP2D6 and codeine metabolism⁹. Drug and/or dosage response are then predicted. International guidelines have been published and are often referred to on reports¹⁰.

WHAT ARE THE BENEFITS OF DIRECT-TO-CONSUMER GENETIC TESTING?

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 study results are conflicting^{11,12}
- Provide useful information for medication choice 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 e.g. cystic fibrosis, sickle cell anemia
- Reveal increased risk of an adult-onset disorder with published screening and surveillance guidelines e.g. alpha-1 antitrypsin deficiency, BRCA-associated hereditary breast and ovarian cancer

WHAT ARE THE LIMITATIONS AND RISKS OF DIRECT-TO-CONSUMER GENETIC TESTING?

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^{13,14}
- **Family health history-based risk assessment is still the gold standard in the initial assessment for heritable conditions¹⁵**

RELEVANT RESOURCES YOU MAY BE INTERESTED IN:

[Ethnicity-based screening in Canada](#) point of care tool

[Expanded carrier screening](#) point of care tool

[Alzheimer disease](#) GEC-KO on the run

[Multiple sclerosis](#) GEC-KO on the run

[Hereditary breast and ovarian cancer syndrome](#) GEC-KO on the run

[Lynch syndrome](#) (formerly hereditary non-polyposis colorectal cancer syndrome) GEC-KO on the run

More information about DTC-GT in Canada, references and additional resources can be found at www.geneticseducation.ca > GEC-KO Messenger > Direct to consumer genetic testing.

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