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Direct-to-Consumer Genetic Testing (DTC-GT)

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Abstract

Direct-to-consumer testing (DTC-GT) is a new model of genetic service delivery available to consumers without the intermediary of a health care professional. Companies marketing such a service model highlight only the benefits without stressing on the potential drawbacks of such a system. In this brief review, we describe the potential benefits and concerns of DTC-GT.

Introduction

Genetic tests identify changes in chromosomes, genes, or proteins and help to confirm or rule out a genetic condition. They also aid in determining a person's chance of developing or passing on a genetic disorder. The most common and widely accepted model of delivery of genetic testing is in a clinical setting, under the guidance of a genetic healthcare professional, after appropriate pre-test counseling and informed consent. Appropriate post-test counseling is also provided after the return of results wherein the implications of the results are explained along with further plan of action. Increasing media coverage about genetic research and testing has made people aware and interested in learning more about their own genetic make-up. This "genetic curiosity" of healthy individuals has given rise to a new branch of genetic testing services called "direct-to-consumer genetic testing (DTC-GT)". Though this genetic testing service model may look highly lucrative and empowering, there are many potential drawbacks. This review is aimed to give more information about delivery of these services and highlight a few caveats associated with it.

What is DTC–GT?

It is over-the-counter genetic testing available directly to consumers through private companies. It has moved genetic testing from the clinics into the comforts of the consumers' homes. The test kits can be bought online or in a pharmacy (in the west). These tests are marketed as enabling and informative tools allowing consumers to access information on their genetics, without the involvement of a trained medical genetics professional.

Why do people opt for DTC–GT?

The demand for DTC-GT is on constant rise owing to inadvertent advertisements and publicity gimmicks evoking the curiosity of healthy, aware and ready-to-pay individuals.

1. Curiosity: Consumers claim curiosity about their past (ancestry testing), present (traits and characteristics) and future (predictive testing), as major motivators for uptake of DTC-GT (Su, 2013).

2. Recreation / infotainment: Many companies propose a relationship between an individual's genomic makeup and lifestyle aspects like nutrition (nutrigenomics), fitness, alcohol preferences, skin care, and athletic abilities (Su, 2013). Companies also provide products and programs to modify consumers' lifestyle according to the results. Consumers also use these tests to find the intellectual, behavioural, creative and athletic traits in their children.

3. Concerns of the 'healthy and worried well': DTC-GT is marketed as helpful in reproductive decision making and providing preventive or management interventions for apparently healthy individuals. People with no family history of genetic conditions and unremarkable personal health histories inadvertently worry about their potential health risks and use these tests (Schimdt et al.,2019).

4. Specific concerns about family history of genetic diseases: Individuals with a family history of genetic conditions, especially multifactorial conditions like Alzheimer disease, cancers, diabetes or

heart disease may express curiosity, worry, and/or anxiety and would like to know their risks for the same (Schimdt et al.,2019).

5. Individuals with non-specific symptoms in search of a specific diagnosis: Highly anxious individuals with non-specific symptoms would do genetic testing to find an answer to their symptoms.

What are the service delivery models available?

There are currently two service delivery models for DTC-GT:

• **Direct-to-consumer** – In this commercial model, consumers can undertake a test without any involvement of a healthcare professional. The tests are directly advertised, sold and delivered to the consumer.

• **Consumer-directed genetic testing (CD-GT)** – These tests are directly advertised to the consumers, but the tests have to be ordered by a healthcare professional and/or the results have to be returned to a healthcare professional. However, an independent third-party healthcare provider, who is not trained in medical genetics, can also act as the ordering physician and the treating doctor may not be involved directly. The consumers research the test options and request the healthcare professional for a specific test (Ramos et al., 2018).

These models are constantly being updated with newer services and genetic information being added to increase the consumers' uptake. DTC-GT companies have started providing access to in-house or contracted genetic counsellors for post-test result interpretation, counseling and giving further plans of action. Genetic counseling is integrated in the test price in some or charged separately in some models of service delivery (Ramos et al., 2018).

What are the potential benefits?

Advocates of DTC-GT argue that it is an empowering tool which enhances the autonomy of consumers by giving them the right to own and use their genomic information to make health and lifestyle decisions. It allows them to be in charge of their healthcare management, without the intermediary of doctors and long waiting lists for hospital appointments (Eissenberg, 2017). It is also claimed that these tests can increase awareness about genetic disorders and disease predispositions among a larger number of individuals (Su, 2013). This in-turn could lead to advanced research in the field of personalized medicine and improved public healthcare.

What are the concerns of DTC–GT?

Issues in DTC-GT arise at every step of service delivery from advertising to the return of the report.

1. Marketing and advertising: Emotional language, appealing designs, testimonials from affluent individuals and exaggerated positive claims of empowerment over one's health are used by almost all the DTC-GT companies as their major marketing strategy. These may affect the consumers' impression of value of the product, its actual need and usefulness for them (Niemiec et al., 2017).

2. Pre-test counseling and informed consent: DTC-GT consumers do not know what to expect from the results due to lack of pre-test counselling. Also the consumer on purchase of the services signs a consent form, but there is no healthcare professional intermediary to discuss and highlight the utility and limitations of the tests, potential results, their implications, storage and future use of their genomic data.

3. Clinical utility, validity of the test and interpretation of results: The scientific evidence for clinical utility of many tests offered is very limited, especially for complex traits. These tests emphasise only on the genetic cause of a condition, totally disregarding the effects of environment, medical and family history and lifestyle of the consumers. Clinical validity of the identified variants is also difficult to prove. All clinically relevant variants or even genes may not be included in analysis. Many DTC-GT companies lack involvement of clinically trained healthcare scientists or genetic professionals for variant interpretation. It is also unclear whether all DTC-GTs are performed in certified laboratories.

There exists a high degree of variability in testing methods between DTC-GT companies. Some use single nucleotide polymorphisms (SNPs) for finding associations between genetic makeup and traits or disease predisposition, while some of the companies use next generation based techniques (whole exome or whole genome sequencing) to find exact variants leading to genetic predispositions. This leads to variability in interpretation and possibility of conflict in risk interpretations (Tandy-Connor et al., 2018). The information

provided in the DTC-GT reports is often in terms of a percent increase in risk (eg, "30% more likely") with no additional details and information about the background risk on which this risk is based. Such estimates can be misleading, especially if the background risk for a condition is low (<1%), which could lead to unnecessary panic. Age-dependent penetrance of certain conditions may also be difficult for consumers to gauge and may lead to false reassurance if negative for those conditions.

The result may not always be positive or negative. There is also a chance of receiving variants of unknown significance (VUS), whose clinical validity is extremely difficult to prove and interpret and is even more difficult for the consumer to understand and use this information without the help of a qualified genetic healthcare professional.

4. Medical actionability: Consumers are clueless about the meaning and implications of the results returned to them and they can be misled into believing that the information they receive is medically actionable They do not realize that these are only predicted and not exact risks. No post-test counseling to explain the results further complicates this issue. This may lead to medical mismanagement wherein consumers may take a serious decision about treatment (prophylactic surgery based on *BRCA* variants), lifestyle choices or inappropriate dosage adjustment (following a pharmacogenomic test report).

5. Psychosocial impact: It may also cause serious psychological distress to the consumers who may not be prepared for bad news and may experience anxiety, emotional trauma, guilt, anger, denial or depression (Roberts et al., 2013). It may also cause distress to other family members who do not wish to know about their genetic risks for disease but now are incidentally found to be at-risk because their relative chose to undertake DTC-GT without proper guidance.

6. Third party interpretations, data storage and privacy: Various third party applications claim to retrieve information from the DTC-GT raw data. This can cause serious problem with variant interpretations, actionability and quality due to inexperience and reliability of the scientific evidence to prove the variant to be pathogenic (Niemiec et al.,2017).

7. Carrier testing and testing of minors: Carrier testing results have a huge impact on a couple's reproductive choices and if not validated or interpreted appropriately, may have adverse effects on it (on their having children or abortion). Testing of asymptomatic minors for traits or even disease predispositions or carrier testing which has implications only for reproductive decisions has multiple ethical, legal and social issues is not considered ethical (Phadke & Gowda, 2013). It takes away the basic autonomy of the child to know about his/her genetic make-up. It can also lead to undue pressure on the child and psychological distress, stigmatization, discrimination (in schools, for insurance, employment) and need to undergo unnecessary medications or interventions.

8. Regulations: There are no regulations on genetic testing, especially on DTC-GT, in India. Hence the quality of reports can be highly questionable.

9. Ancestry and paternity testing: These tests can lead to unexpected results revealing false paternity or unknown sibships. This information may be distressful for some individuals and can have serious impact on the family dynamics.

Genetic counselors' view on DTC–GT

Genetic counseling is considered the gold standard of care when conducting diagnostic genetic testing. To not offer that in the setting of DTC-GT is a deviation from that standard of care.With increase in awareness of the consumers about the need to understand the DTC-GT results, some of the companies have started offering post-test counseling (Ramos et al., 2018). However, there are limited services to make sure that the information is fully understood by the consumer. Appropriate pre- and post-test counseling is rarely offered directly by DTC-GT companies and is inconsistently accessed by consumers when available (Harris et al.,2013) .In a study by Hock et al. 2011, to assess genetic counselors' knowledge and belief about DTC-GT, about 50% of the counsellors felt DTC-GT was acceptable if genetic counseling was provided and they also agreed that they had a professional obligation to be knowledgeable about DTC-GT. The other 50% of respondents thought that genetic testing should be limited to clinical settings. This clearly indicates a disparity among the counselors and their view on their role in managing DTC-GT consumers.

Position statements from professional bodies

Several professional bodies like American College of Medical Genetics and Genomics (ACMG), National Society of Genetic Counselors (NSGC), American Society of Human Genetics (ASHG)

(Hudson et al.,2007), European Society of Human Genetics (ESHG), American College of Obstetricians and Gynaecologists (ACOG) and US Food and Drug Administration (FDA) have issued position statements on DTC-GT. Society of Indian Academy of Medical Genetics has issued a position statement on DTC-GT on August 10, 2019. They all express concerns about the limitations of tests, communication of results, impact of genetic test results, unpreparedness of consumers for results, lack of information about recommended follow-up, psychological distress and privacy of genetic data. They unanimously recommend undertaking of genetic testing under the guidance of a knowledgeable genetic healthcare professional or genetic counsellor before pursuing DTC-GT. They encourage consumers to be skeptical of these tests' claims and realise that DTC-GT results can have important health implications for individuals and family members. They also insist that the DTC-GT company websites should clearly mention about the limitations and probabilistic nature of the tests – what they can and cannot detect, in an understandable manner. They must also address the privacy and confidentiality concerns regarding consumers' genetic data.

These statements however hold a diplomatic stance on DTC-GT. Only ACOG discourages the use of DTC-GT due to the potential harm of misinterpretation or inaccurate result.

Many professional bodies have criticized the clinical validity and utility of the health-related information provided and expressed concerns about negative downstream consequences on misinterpretation of this information by the consumers or their primary health-care providers. All the professional bodies unanimously and strongly discourage the use of DTC-GT for children due to lack of regulation on test content, accuracy and interpretation along with loss of autonomy of the child. Genetic tests if needed for a minor should be clinically indicated (for diagnosis and health-altering management) and be ordered only by a healthcare professional who will be responsible for subsequent management.

Conclusion

DTC-GT has very much arrived into the genetic testing market. Literature suggests that DTC-GT is neither as empowering as claimed nor as harmful as feared. However, before and after deciding to purchase a test, it is important for the consumers to understand the harms and benefits of the applications marketed or the actionability of results obtained. DTC-GT cannot sufficiently substitute traditional genetic testing without the expert guidance of a genetic professional.

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