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Ethical issues in consumer genome sequencing: Use of consumers' samples and data

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ABSTRACT

High throughput approaches such as whole genome sequencing (WGS) and whole exome sequencing (WES) create an unprecedented amount of data providing powerful resources for clinical care and research. Recently, WGS and WES services have been made available by commercial direct-to-consumer (DTC) companies. The DTC offer of genetic testing (GT) has already brought attention to potentially problematic issues such as the adequacy of consumers' informed consent and transparency of companies' research activities. In this study, we analysed the websites of four DTC GT companies offering WGS and/or WES with regard to their policies governing storage and future use of consumers' data and samples. The results are discussed in relation to recommendations and guiding principles such as the "Statement of the European Society of Human Genetics on DTC GT for health-related purposes" (2010) and the "Framework for responsible sharing of genomic and health-related data" (Global Alliance for Genomics and Health, 2014). The analysis reveals that some companies may store and use consumers' samples or sequencing data for unspecified research and share the data with third parties. Moreover, the companies do not provide sufficient or clear information to consumers about this, which can undermine the validity of the consent process. Furthermore, while all companies state that they provide privacy safeguards for data and mention the limitations of these, information about the possibility of re-identification is lacking. Finally, although the companies that may conduct research do include information regarding proprietary claims and commercialisation of the results, it is not clear whether consumers are aware of the consequences of these policies. These results indicate that DTC GT companies still need to improve the transparency regarding handling of consumers' samples and data, including having an explicit and clear consent process for research activities.

1. Introduction

Direct-to-consumer (DTC) genetic testing (GT) companies operating outside of the traditional healthcare system have attracted numerous critiques of their practices over the last decade (Kalokairinou et al., 2014). Beyond questioning the clinical validity and utility of the tests, the appropriateness of medical supervision and genetic counselling, some of the concerns centre on the storage and use of consumers' samples and data. These include a number of inter-related issues such as what consumers are told (e.g., during the consent process) about storage and use of samples and data; proprietary claims stemming from secondary uses of sample and data; as well as the coupling of companies' genetic testing offer with research activities. Indeed, an earlier explorative study of DTC GT companies has shown that for some companies the consent to participation in research may not be adequate; it questioned whether the information provided by the companies about their research activities was clear and explicit enough for consumers to understand what they were agreeing to (Howard et al., 2010). Furthermore, it highlighted that such ambiguous presentations of information for testing and research activities blur the lines between consumers and research participants, undermine the informed choice of consumers and may potentially undermine public trust in research in general (Howard et al., 2015, 2010).

Recent advancements in sequencing technologies have resulted in a significant decrease in the price of whole-exome and whole-genome sequencing (WES, WGS), which has allowed for a greater use of these approaches in both the clinical and research domains causing a shift in testing approach from analysing one or a few genetic variants to the study of an entire exome/genome sequence. WES/WGS generates an unprecedented amount of sensitive health-related genomic data useful in healthcare management and powerful in the research setting (Rabbani et al., 2014). While much of the discussion surrounding the ethical, legal and social implications (ELSI) of these high-throughput approaches has been focused on these settings, much less attention has been paid to commercial companies offering sequencing services DTC.

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Table 1
Information on the companies, their WES/WGS services, model of provision of testing, and the website documents studied.

Company name & country	Description of service	Model of provision of testing	Sections of the websites studied
Illumina, USA	WGS: TruGenome Undiagnosed Disease Test — "*intended to provide information to physicians to aid in the diagnosis of inherited diseases of single-gene etiology (Mendelian diseases)*". TruGenome Predisposition Screen — "*analysis and interpretation are performed on 1691 genes that have well-established associations to a set of 1232 conditions (…), and 11 medically actionable genes associated with response to 16 different drugs*" TruGenome Technical Sequence Data — "*whole-genome sequencing data in two formats: a gVCF and a BAM*" (http://www.illumina.com/clinical/illumina_clinical_laboratory/trugenome-clinical-sequencing-services.html)	"*TruGenome Clinical Sequencing Services…must be ordered by a licensed physician*" (http://www.illumina.com/clinical/illumina_clinical_laboratory/how-to-order.html)	Informed Consent (different form for each test)
GeneYouIn, Canada	WES: VitaSeq™: "*With VitaSeq™, assess your risk of cancer, heart disease, autoimmune or neurological diseases.*" PregnaSeq™: "*With PregnaSeq™, genetic testing can help you optimize your fertility treatment and find out if you and your partner are at risk for passing on preventable diseases.*" (https://www.geneyouin.ca/)	A health care professional is not required for test ordering (although 30 minute phone consultation is required before ordering) (https://www.geneyouin.ca/how-it-works/how-to-order/)	Informed Consent, Terms and Conditions
Gene By Gene, USA	WES/WGS — raw data or with "*alignment and variant calling*" (https://www.genebygene.com/pages/research#) or (only for WES) with "*professional RUO* [research use only] *interpretation*" (https://www.genebygene.com/pages/research?goto=whole-exome-with-interpretation#)	For Clinical Testing service a clinician orders the test (https://www.genebygene.com/pages/genetics#how-to-order); information not available for "Research and Consumer" services	Terms and Conditions
Inneova, Canada	WGS — "*screening risk factors and sensitivity to particular molecules which can help a client's physician recommend specific check-ups as well as optimize the administration of medications and diets*" (http://www.inneova.com/tout.php)	"*we accept test requests from licensed medical professionals only*" (http://www.inneova.com/tout.php)	Statement of consent, Disclaimer and privacy policy

Given that WES/WGS is likely to become increasingly more available and there is the potential for these services to be coupled with research activities using consumers' data (http://www.technologyreview.com/news/540711/inside-illuminas-plans-to-lure-consumers-with-an-app-store-for-genomes/), the ELSI of DTC genomics are particularly important to address now. We therefore studied the websites of companies advertising WGS and/or WES DTC to shed light on the information they provide to consumers. More specifically, we analysed webpage documents that consumers should sign and/or agree to when undertaking the test (i.e., depending on the company, sections entitled informed consent, terms and conditions, statement of consent, disclaimer and privacy policy; Table 1). We focused on information relevant to storing and using consumers' data and samples. These issues include: i) purpose and period of samples and data storage; ii) consumer consent; iii) data access and sharing; iv) identifiability and confidentiality of data; and v) proprietary claims. Four companies were identified (circa mid-2015) which offer and/or advertise WES and/or WGS DTC: Illumina, Gene by Gene, GeneYouIn, and Inneova. Each stated that they offer WGS and/or WES, although the scope and focus of data analysis and interpretation varied from providing only raw sequencing data to the diagnosis of Mendelian disorders. Moreover, they had different models of provision (e.g., with or without physician referral; Table 1). We defined direct-to-consumer genetic/genomic testing as the offer and/or advertisement of testing direct-to-consumers. We considered companies that required a health care professional to order the WGS or WES services also as DTC companies since they were still advertising directly to consumers, and this can have a significant impact on the demand and ultimate use of a product or service. This is congruent with the scope of DTC GT given by the UK Human Genetics Commission, which included situations where "*tests are commissioned by the consumer but where a medical practitioner or health professional is involved in the provision of the service*." (Human Genetics Commission, 2010).

2. Purpose and period of samples and data storage

Three of the four analysed DTC companies (Illumina, Gene By Gene, GeneYouIn) stated on their websites that they may use consumers' data and/or samples for purposes beyond performing the genetic test ordered by the consumer (Table 2). Illumina stated that "*leftover specimen and results may be used by Illumina for purposes of quality control, laboratory operations, and laboratory improvement*" (http://www.illumina.com/content/dam/illumina-marketing/documents/clinical/forms/form-test-req-predisposition.pdf). This suggested that the company performs internal quality assurance, for which specific consent is not necessarily required as long as some conditions are met (e.g., actively informing individuals of this use; Royal College of Physicians et al., 2011; The Human Tissue Authority, 2004). The period for which the results and specimen would be stored was not specified in the analysed document.

Meanwhile, GeneYouIn indicated that it would store the samples for 90 days and that after this period they would be discarded; the company did not specify the period for data storage. GeneYouIn also stated explicitly that it may use consumers'[1] data for research, providing a general description of the type of research on its informed consent page:

> "*You provide your consent for research in which we analyse your genetic data and phenotype information in order to discover or validate associations between certain genetic variations and diseases.*"
> [https://www.geneyouin.ca/informed-consent]

Gene By Gene indicated in its terms and conditions that it would store consumer data for 30 days or longer; after this time the data

[1] The companies GeneYouIn and Gene By Gene use a word "customer" in the analysed texts. However, as implied in these texts, a customer (meaning a person who buys a test) is simultaneously a consumer (meaning a user of a test). Therefore, we use the word "consumer" throughout this article, also when referring to the quotations on the webpages of GeneYouIn and Gene By Gene.

Table 2
Information about the purpose and period of samples and data storage.

Company name	Quotes concerning purpose and period of samples and data storage	Period of storage	Information about research activities
Illumina	Informed consent[a]: "*Pursuant to best practices and clinical laboratory standards, leftover specimen and results may be used by Illumina for purposes of quality control, laboratory operations, and laboratory improvement. All such uses [will be de-identified]*, and in compliance with applicable law.*" *the phrase found only in the informed consent for TruGenome Predisposition Screen	Not available	Not available
GeneYouIn	Informed consent[a]: "*You provide your consent for research in which we analyze your genetic data and phenotype information in order to discover or validate associations between certain genetic variations and diseases. These studies will improve the accuracy of our predictions for you and other customers. As the number of our customers grows, our ability to study their combined genetic data and phenotype information further advances scientific and medical research, thus improving health care.*" Terms and conditions[a]: "*Your genetic data will be stored in Your Account, and you appoint GeneYouIn as a custodian of your genetic and health data. By accepting these Terms you agree that your anonymized genetic and health data can be used for research purposes. (…) All biological samples and DNA will be destroyed after 90 days following obtaining the test results, however the information of your genetic code will be stored in Your Account, and you appoint GeneYouIn as a custodian of your genetic and health data. By accepting these Terms you agree that your anonymized genetic and health data can be used for research purposes.*"	Samples — 90 days; data — not available	Research may be performed on consumers' data
Gene By Gene	Terms and conditions[a]: "*Any sample material sent will be used only to perform the specifically ordered testing. After testing is complete, remaining sample material is stored for 180 days, unless otherwise specified by regulatory agencies. After 3 months, the sample will be discarded or de-identified and retained for in-house laboratory use. (…)The customer specifically understands that they will not receive compensation for any research or commercial products that include or results from your sample, results, or personal record*".	Data — 30 days or longer; samples — unclear: at least 90 or 180 days	Contradictory statements: research will not be performed on consumers' samples and research may be performed on consumers' samples and data (inexplicit statement)
Inneova	Disclaimer and privacy policy[a]: "*The DNA is used only for the purpose of predictive genetics testing. Once processed, each DNA sample is discarded following a secure protocol.*"	Samples — discarded after testing; data and results — not available	No research on consumers' DNA samples; no information about research on data

[a] These denote the specific documents/sections of websites where the quotes can be found.

might be permanently deleted, however, the consumer could request storage for a longer period. Regarding the storage of the samples, the company indicated: "*After testing is complete, remaining sample material is stored for 180 days, unless otherwise specified by regulatory agencies.*" However, in the following sentence it stated: "*After 3 months, the sample will be discarded or de-identified and retained for in-house laboratory use*", making it unclear for what period the samples would be actually stored. Furthermore, Gene By Gene provided a few statements concerning the use of samples and data that appear contradictory: "*Any sample material sent will be used only to perform the specifically ordered testing.*" Meanwhile, a few paragraphs below on the same page, it was written: "*After 3 months, the sample will be discarded or de-identified and retained for in-house laboratory use.*" And: "*The customer specifically understands that they will not receive compensation for any research or commercial products that include or results from your sample, results, or personal record*" (https://www.genebygene.com/pages/terms). The last two statements imply that consumers' samples and data may be involved in research beyond quality assurance, which, without further information, appears to contradict the first statement that samples would be used only for the ordered testing. This information is ambiguous and confusing.

The fourth company studied, Inneova, stated that biological samples would be destroyed after performing the test, but did not describe what would happen to the data.

The incomplete information provided by the companies regarding the storage and use of consumers' data and samples is incongruent with the "Statement of the ESHG (European Society of Human Genetics) on direct-to-consumer genetic testing for health-related purposes" (called further the Statement of the ESHG), which recommends that companies should "*explain what will happen to the sample and the data when the testing process is concluded*". Furthermore, in case of research activities being performed on the consumers' data or samples, the ESHG (2010) recommends that more detailed information should be provided: "*Informed consent documents for participation in research should disclose the procedures for storing and disposal of samples and genetic information, the time period and conditions for storing them*" (European Society of Human Genetics, 2010). In addition, DTC GT companies should "*have a clearly laid-out plan as to what will happen to the samples and data should the company be sold or go bankrupt*" (European Society of Human Genetics, 2010). None of the web-documents/webpages studied from these four companies provided a description of what will happen in such situations. This echoes results of a study of DTC GT companies conducted by Zawati et al., 2011, in which the authors called for "clearer institutional frameworks on the issue of closure."

Overall, our results show that two companies indicated may perform research on consumer data and/or samples, while two other companies did not make reference to research activities. Furthermore, only one company specified the period of storage for data, while the period of storage for samples was stated clearly by two of four companies. None of the companies made reference to what would happen if the company were sold or went bankrupt.

3. Consumer consent

3.1. Consent for services

Based on the websites studied, consumers give their consent for the services purchased, including agreeing to the information in the aforementioned documents by ordering the test (https://www.geneyouin.ca/

terms-conditions/; https://www.genebygene.com/pages/terms; http://www.inneova.info/contenu.php?page=disclaimer.php) or by signing the form which is sent to the company together with the sample for analysis (http://www.illumina.com/content/dam/illumina-marketing/documents/clinical/forms/form-test-req-predisposition.pdf). In the case of the informed consent from GeneYouIn, it was not made explicit how exactly consumers provide consent to the testing (e.g., via signature, a verbal agreement)

> "*We ask you to provide your informed consent to ensure that, before purchasing GeneYouIn's genetic testing and consulting services, you are not only aware of the benefits, but also understand the limitations and potential risks. Please carefully review the information described below before you purchase any of our services.*"
>
> [https://www.geneyouin.ca/informed-consent/]

The provision of information and the manner of consenting in the DTC GT context may raise the question of whether consumers have read and fully understood the information to which they agree and thus whether their decision is truly an informed decision. The low readership of sections such as the "terms of service" has already been discussed in the context of online transactions e.g. when purchasing software (Maronick, 2014). However, as noted by the Presidential Commission for the Study of Bioethical Issues (2013), by providing health information DTC GT companies "*interact in both the business and medical realms, and could find themselves subject to the ethical principles pertinent to business transactions as well as those of medical care*". Therefore, DTC GT companies, depending on the types of tests they sell, can be subject to the e-commerce legal framework, as well as fall within the scope of ethical requirements related to genetic testing in the clinic context and/or in the realm of research participation. One of these requirements is to obtain informed consent for testing and research, which has different functions than the terms of service of a consumer contract (Bunnik et al., 2014). The informed consent process involves providing consumers certain types of information about testing (e.g. benefits and risks) in an understandable manner. Furthermore, as explained in the Statement of the ESHG the process of informed consent should "*ensure that individuals understand the disclosed information, are legally competent and cognitively capable of acting without external pressure, and give their agreement to all the elements involved.*" (European Society of Human Genetics, 2010). It should also protect against involuntary testing (Bunnik et al., 2014).

3.2. Consent to research

The information about the possibility of performing research on consumers' samples (i.e., for the companies GeneYouIn and Gene by Gene) was not included on the front pages of the companies' websites or the main pages including the description of what the companies offer (Table 1). Therefore, it is not clear whether the consumers have been aware of the companies' research activities and if they have been genuinely consenting to them. Furthermore, the provision of information about research activities raises concerns about clarity and understandability of this information for consumers, as mentioned earlier. This type of unclear and non-explicit way of "recruiting" consumers as research participants appears to be in contradiction of the requirement for informed consent. The importance of informed consent for research has been articulated by various guidelines and legal documents, for instance the Statement of the ESHG specifies: "*If samples or data are to be used in any research, this should be clear to consumers, and a separate and unambiguous consent procedure should take place.*" (European Society of Human Genetics, 2010). This recommendation underlies another concern about the adequacy of consent for research activities of the companies, namely the presence of a separate consent procedure. This practice has been acknowledged and supported as it "*enhances autonomy by drawing the customer's attention to the change in the use of their samples and data*" (Tobin et al., 2012). Neither of the two companies that may conduct research and were examined here offered a separate informed consent form for research. What is even more troubling, they also did not provide a possibility to opt-out of their potential research activities, which has been criticised as a practice undermining the autonomy of consumers (Tobin et al., 2012).

3.3. Additional information needed in the consent process

The recommendations for informed consent for research specify that besides information regarding the destination of the consumers' data and samples after performing the test, the consent should include additional elements. For example, the ESHG states:

> "*Informed consent documents for participation in research should disclose the procedures for storing and disposal of samples and genetic information, the time period and conditions for storing them, inform participants of the identity of any third parties who may be granted access to data or samples, and include also information on the fact that the research may lead to commercialization and patents, on any customers' rights to commercial benefits and on the property of biological samples and data.*"
>
> [European Society of Human Genetics (2010)]

The Global Alliance for Genomics and Health suggests similar types of information to be provided in order to respect the responsible sharing of genomic and health-related data in general, and specifically to support the principle of transparency:

> "*Provide clear information on the purpose, collection, use and exchange of genomic and health-related data, including, but not limited to: data transfer to third parties; international transfer of data; terms of access; duration of data storage; identifiability of individuals and data and limits to anonymity or confidentiality of data; communication of results to individuals and/or groups; oversight of downstream uses of data; commercial involvement; proprietary claims; and processes of withdrawal from data sharing.*"
>
> [Knoppers (2014)]

Similarly, the recommendations on WGS issued by the US Presidential Commission for the Study of Bioethical Issues suggest the presence of particular elements in informed consent, which also apply to commercial WGS:

> "*Researchers and clinicians should evaluate and adopt robust and workable consent processes that allow research participants, patients, and others to understand who has access to their whole genome sequences and other data generated in the course of research, clinical, or commercial sequencing, and to know how these data might be used in the future. Consent processes should ascertain participant or patient preferences at the time the samples are obtained.*"
>
> [Presidential Commission for the Study of Bioethical Issues (2012)]

In the remainder of this article we discuss some of the elements that have been highlighted in the above documents as being important to communicate to persons undergoing genetic or genomic testing.

4. Data access and sharing

All companies stated that they may grant access to consumers' data to a third party that is legally authorized or if it is required by law (e.g., by a court order) (Table 3). Illumina, GeneYouIn and Gene By Gene also specified that, with the consumer's consent, they may grant access to the healthcare provider to whom the test results would be released. In addition, GeneYouIn indicated that consumers may withdraw this type of consent and request deletion of their records. Moreover, the company specified that it might share consumers' data with research

Table 3
Information about consumers' data access and sharing.

Company name	Information on data access and sharing
Illumina	Informed consent[a]: "*Illumina keeps test results confidential. Illumina will only release your test results to your healthcare provider, his or her designee, other healthcare providers involved in your medical care, or to another healthcare provider as directed by you (or a person legally authorized to act on your behalf) in writing, or otherwise as required or authorized by applicable law.*" (http://www.illumina.com/content/dam/illumina-marketing/documents/clinical/forms/form-test-req-predisposition.pdf)
GeneYouIn	Informed consent[a]: "*You authorize GeneYouIn to use and share your anonymized genetic and clinical data with research organizations. If you decide that you do not want us to share your anonymized genetic and clinical data, please initial the check box next to this bullet point.* ☐ *(…) Please note that GeneYouIn will not disclose your health information without your explicit consent or a legal order. (…) Through our electronic tools, you can grant your physician or other trusted health care provider secure access to your report. If at any time you decide to withdraw your consent, you may request deletion of your records.*" (*https://www.geneyouin.ca/informed-consent*) Terms and conditions[a]: "*Access to you biological sample and health data by a court-appointed order will be granted according to the Privacy laws of Canada and Ontario.*" (https://www.geneyouin.ca/terms-conditions/)
Gene By Gene	Terms and Conditions[a]: "*Test results will be released only to the ordering clinician or genetic counselor. Gene By Gene, LTD will not release results to a third party without proper authorization in accordance with the Health Insurance Portability and Accountability Act (HIPSS) of 1996. (…)The customer understands that by providing any sample, having your sample processed, accessing results, or providing personal information, that the customer acquires no rights in any research or commercial products or services that may be developed by Gene by Gene, LTD. or its collaborating partners." (…) "The customer understands that Gene By Gene, LTD. is not responsible for misuse, mishandling, or misrepresentation of this data by the customer or other third parties who have been given rightful access to the aforementioned data or materials.*" (https://www.genebygene.com/pages/terms)
Inneova	Statement of consent[a]: "*I understand that ICL will not disclose my identity, contact details, or test results to third parties (except to its medical, scientific, and other service partners, subsidiaries and related business entities, legal advisors, agents, or appointees for the purpose of performing genetic testing or interpretation services, as well as any associated administrative transactions, as deemed necessary by ICL in the normal course of business under the terms of this Agreement as well as under its Disclaimer and Privacy Policy). I understand that ICL will be absolved of this responsibility to a limited extent as stated in its Disclaimer and Privacy Policy in the case of any legal action, court order, or legislation requiring it to do otherwise.*" (http://www.inneova.com/contenu.php?page=terms.php)

[a] These denote the specific documents/sections of websites where the quotes can be found.

organizations and that consumers would have an opportunity to opt-out of their data sharing by checking a box in the informed consent.

Inneova, although somewhat indirectly, also mentioned the possibility of sharing data:

> "*I understand that ICL will not disclose my identity, contact details, or test results to third parties (except to its medical, scientific, and other service partners, subsidiaries and related business entities, legal advisors, agents, or appointees for the purpose of performing genetic testing or interpretation services, as well as any associated administrative transactions, as deemed necessary by ICL in the normal course of business under the terms of this Agreement as well as under its Disclaimer and Privacy Policy).*"
> [http://www.inneova.com/contenu.php?page=terms.php]

Although the first clause stated no disclosure, the list of exceptions in brackets was long and vague.

Gene By Gene stated that the samples may be "*retained for in-house laboratory use*" and did not specify any third parties with which sharing would happen other than to state that third-party access will only be given with proper "*authorization in accordance with the Health Insurance Portability and Accountability Act*". However, the statement "*The customer understands that by providing any sample (…) or providing personal information, that the customer acquires no rights in any research or commercial products or services that may be developed by Gene by Gene, LTD. or its collaborating partners.*" (https://www.genebygene.com/pages/terms) suggests that consumers' data, in some way, may be indeed, used by "collaborating partners" and hence shared in some way.

Importantly, the companies did not specify the detailed conditions (except mentioning "legal authorization") under which third parties would gain access to consumer data. Also lacking was information regarding whether the transfer of data would be international and information about oversight of downstream uses of data, both of which are elements suggested in the "Framework for responsible sharing of genomic and health-related data" (called further Global Alliance Framework) in order to respect and support transparency in data sharing (Knoppers, 2014). Similarly, the Presidential Commission for the Study of Bioethical Issues recommends:

> "*Funders of whole genome sequencing research; managers of research, clinical, and commercial databases; and policy makers should maintain or establish clear policies defining acceptable access to and permissible uses of whole genome sequence data. These policies should promote opportunities for models of data sharing by individuals who want to share their whole genome sequence data with clinicians, researchers, or others.*"
> [Presidential Commission for the Study of Bioethical Issues, 2012]

Although both of these documents highlight the importance of sharing data for maximising research potential, and they encourage making data accessible to researchers, they also stress that sharing should be conducted in a responsible way. Based on our findings, this may not be fully respected by some DTC WGS companies.

5. Data security: identifiability and confidentiality

All four companies stated that they provide privacy safeguards for consumers' samples and/or data (Table 4). Illumina stated that consumers need the code provided to their healthcare practitioner in order to access their results. Meanwhile, GeneYouIn described generally that it employs "*commercially validated and reasonable computational and organizational safeguards*" (https://www.geneyouin.ca/terms-conditions/). Similarly, Gene By Gene stated that it "*implements administrative, physical and technical safeguards to secure our client's protected health information as defined by HIPAA*" (https://www.genebygene.com/pages/terms). Furthermore, Illumina, Gene By Gene and Inneova specified that the samples and/or data would be de-identified. GeneYouIn stated specifically that consumers' genetic and health data would be anonymised. The information provided by the companies seemed, at least to some extent, to fulfil the requirement articulated by the Statement of the ESHG: "*companies offering DTC genetic tests should preserve the customer's privacy, keep their data confidential, inform them about their security procedures (…).*" (European Society of Human Genetics, 2010). They also concur with the recommendations of the PCSBI which states that "*Accessible whole genome sequence data should be stripped of traditional identifiers whenever possible to inhibit recognition or re-identification*" (Presidential Commission for the Study of Bioethical Issues, 2012). The Global Alliance Framework, additionally, suggests provision of information about "*limits to anonymity or confidentiality of data*" (Knoppers, 2014). GeneYouIn, Illumina and Gene By Gene stated that there are limitations to the privacy safeguards, which may be breached by, for example, the use of malicious software (Table 4). Yet information about the possibility of re-identification of anonymised genomic data was missing from the web documents/webpages studied for

Table 4
Information on samples' and data identifiability and confidentiality.

Company name	Samples' and data identifiability and confidentiality
Illumina	Informed consent[a]: "*You will need to obtain a unique code from your doctor to download your test results. (…) The Internet and wireless services may not be 100% secure. There is always a risk that you may lose the device or the security on the device may be breached and someone else may then gain access to your test results. (…) Discrimination Risks. Genetic information could potentially be used as a basis of discrimination. To address concerns regarding possible health insurance and employment discrimination, many U.S. states and the U.S. government have enacted laws to prohibit genetic discrimination in these circumstances. The laws may not protect against genetic discrimination in other circumstances such as when applying for life insurance or long-term disability insurance. (...) All such uses* [for quality control, laboratory operations, and laboratory improvement] *will be de-identified.*" (http://www.illumina.com/content/dam/illumina-marketing/documents/clinical/forms/form-test-req-predisposition.pdf)
GeneYouIn	Informed consent[a]: "*You authorize GeneYouIn to use and share your anonymized genetic and clinical data (...). The Genetic Information Nondiscrimination Act (known as GINA) was signed into law in May 2008 in the United Sates. This legislation offers federal protection against discrimination based on an individual's genetic information in health insurance and employment settings. While there are different laws in place across the globe that prevent companies from discriminating against people based on race, age, handicaps, and genetic predispositions such laws are not yet fully implemented in Canada.*" (https://www.geneyouin.ca/informed-consent) Terms and Conditions[a]: "*We are not responsible for maintaining security and confidentiality of copies of Your Reports stored outside of GeneYouIn's databases. We are not and cannot be responsible for any personally identifiable information about you that you release on your own, or that you request or authorize us to release. (…) We employ commercially validated and reasonable computational and organizational safeguards against unauthorized disclosure or access to your genetic data or other personally identifiable information about you according to our Privacy & Security Policy. You acknowledge that security safeguards, by their nature, are capable of circumvention and GeneYouIn does not guarantee that your personal identifiable information will not be accessed by unauthorized persons capable of overcoming such safeguards. In particular, our site may be used to access and transfer information, including personally identifiable information about you over the Internet. You acknowledge and agree that GeneYouIn does not operate or control the Internet and that unauthorized users may use malitious software (viruses, worms, trojan horses, and other software) to obtain access to personally identifiable information about you. GeneYouIn will not be liable to you for any damages in connection with unauthorized dissemination of your personal information in accordance with this paragraph.*" (https://www.geneyouin.ca/terms-conditions/)
Gene By Gene	Terms and conditions[a]: "*After 3 months, the sample will be discarded or de-identified and retained (...). However, Gene By Gene, LTD implements administrative, physical and technical safeguards to secure our client's protected health information as defined by HIPAA. (…) Gene By Gene, LTD. will handle all sample specimens in compliance with all applicable laws and regulations. All data received from the customer and data generated will be created, stored, and transferred according to HIPAA guidelines. The customer understands that Gene By Gene, LTD. is not responsible for misuse, mishandling, or misrepresentation of this data by the customer or other third parties who have been given rightful access to the aforementioned data or materials.*" (https://www.genebygene.com/pages/terms)
Inneova	Disclaimer and privacy policy[a]: "*ICL uses a specific tracking system to identify your sample as soon as it enters our facilities. Molecular biologists in charge of your sample do not know who the actual sample belongs to, but only see each sample as a number. This tracking number is associated with your name and contact information only within our secure database, which is not accessible by the lab or anyone outside of our company.*"

[a] These denote the specific documents/sections of websites where the quotes can be found.

all four companies. The relevance of this element for informed consent for genome testing was highlighted by Chow-White et al.:

> "*(…) the consent form should contain language/disclaimer that privacy is not absolutely guaranteed. The unstableness of digital networks and uncertainty of genomic information creates the conditions of privacy without guarantees. The consent form should (…) provide details of data release and sharing, including potential public databases where data could be disseminated and explain the potential of re-identification of anonymized data.*"
>
> [Chow-White et al. (2015)]

Moreover, one may argue that using the term "anonymised" is misleading and disingenuous as it has been shown that anonymised genomic data may be re-identified by linking information from different databases (Gymrek et al., 2013). Indeed, the term "pseudonomisation" may be more accurate in the context of genomic data, however it may be too vague for "lay" consumers to fully understand its meaning. (Moraia et al., 2015). To clarify this issue, companies should explain to consumers that although their data will be stripped of personal information (de-identified) there is still a chance of reidentification.

The Statement of the ESHG also suggests that "*possible consequences related to their [results] disclosure to third parties, such as insurance companies and employers, should be discussed*" (European Society of Human Genetics, 2010). Illumina and GeneYouIn stated that there is a risk of discrimination in case of disclosure of the results (Table 4). Illumina also mentioned the limitations of legal protections against discrimination: "*The laws may not protect against genetic discrimination in other circumstances such as when applying for life insurance or long-term disability insurance.*" (http://www.illumina.com/content/dam/illumina-marketing/documents/clinical/forms/form-test-req-predisposition.pdf). GeneYouIn and Gene By Gene also cited the US Genetic Information Nondiscrimination Act (GINA), which "*prohibits health insurers and employers from discriminating based on genetic information*" (https://www.genebygene.com/pages/terms). Furthermore, GeneYouIn mentioned the limitations of current Canadian law: "*While there are different laws in place across the globe that prevent companies from discriminating against people based on race, age, handicaps, and genetic predispositions such laws are not yet fully implemented in Canada.*" (https://www.geneyouin.ca/informed-consent). Gene By Gene outlined possible consequences of disclosure, including: "*misuse, mishandling, or misrepresentation*" (https://www.genebygene.com/pages/terms).

6. Proprietary claims

GeneYouIn and Gene By Gene stated that consumers would not receive any compensation for being involved in research (Table 5). Gene By Gene also added that a consumer "*will not receive compensation for (…) commercial products that include or results from [customer's] sample, results, or personal record.*"; and "*customer acquires no rights in any research or commercial products or services that may be developed by Gene by Gene, LTD. or its collaborating partners.*" (https://www.genebygene.com/pages/terms). Meanwhile, GeneYouIn explained that it is a custodian of consumers' genetic and health data; however, it did not appear to explicitly outline the implications of this fact. The presence of these elements of information seems to comply with the recommendations of the Global Alliance Framework (Knoppers, 2014) and the Statement of the ESHG, which suggests inclusion of "*information on the fact that the research may lead to commercialization and patents, on any customers' rights to commercial benefits and on the property of biological samples and data.*" (European Society of Human Genetics, 2010).

However, the fact that Gene By Gene consumer's sample could actually *be part* of a commercial product raises particular ethical concerns including whether it is ethically acceptable to sell products that incorporate consumers' samples potentially without providing any benefit-sharing for the consumers (National Health and Medical Research Council, 2011).

In addition, given the concerns about overall adequacy of the consent process for the companies that may conduct research, we can question whether consumers are well informed about potential

Table 5
Information on the proprietary claims found on the studied pages of the companies' websites.

Company name	Proprietary claims
Illumina	Not available
GeneYouIn	Informed consent[a]: "*You understand that you will not receive any compensation as a result of having your DNA analyzed, Your Genetic Data, or your Phenotype Information analyzed, or from any other research performed using your Genetic Data or your Phenotype Information.*" (https://www.geneyouin.ca/informed-consent) Terms and conditions:[a] "*(…) you appoint GeneYouIn as a custodian of your genetic and health data.*" (https://www.geneyouin.ca/terms-conditions/)
Gene By Gene	Terms and conditions[a]: "*The customer understands that by providing any sample, having your sample processed, accessing results, or providing personal information, that the customer acquires no rights in any research or commercial products or services that may be developed by Gene by Gene, LTD. or its collaborating partners. The customer specifically understands that they will not receive compensation for any research or commercial products that include or results from your sample, results, or personal record.*" (https://www.genebygene.com/pages/terms)
Inneova	Not available

[a] These denote the specific documents/sections of websites where the quotes can be found.

commercialisation of research results and their biological material. It has been reported that at least some of the consumers of the DTC GT company 23andMe were not aware of the possibility of commercialising research results, although the company provided a statement about it in its online consent form (Allyse, 2013). Importantly, the information about the potential commercial uses has been shown to be a relevant factor for deciding about whether to participate in research (Gaskell et al., 2012). Therefore, this element of information should be provided to consumers in explicit and clearly understandable form in order to secure their informed choice.

7. Conclusions

Our study of particular sections of companies' websites indicates that some DTC WGS/WES companies might have conducted research with consumer data. Moreover, information about these activities, as well as general information about data and sample storage and specific information about data sharing were found to be lacking. For example, we found multiple instances where disclosures did not comply with guidelines of the ESHG concerning the offer of DTC GT (European Society of Human Genetics, 2010) or with the recommendations outlined in the "Framework for responsible sharing of genomic and health-related data" (Knoppers, 2014). This lack of transparency in the provision of information to consumers could undermine their informed consent. On the bright side, companies were relatively good at providing information about general data security. However, they failed to address the possibility (even if small) of re-identification. Finally, the companies did provide information about proprietary claims and commercialisation.

We recognize that this study is based on a particular set of web documents/webpages sampled at a particular moment in time. As such there is a chance that some of the missing information might have been found elsewhere on the companies' websites. This being said, since the documents we chose are specifically aimed at consumers to read and agree to, we would argue that the necessary information for data and sample storage, secondary use, and potential data or sample sharing should be included in these documents.

Some of the ethical concerns regarding the research practices of DTC WGS companies discussed herein have been raised previously (Gibson and Copenhaver, 2010; Howard et al., 2015). Furthermore, earlier this year, it was reported that the DTC GT company 23andMe together with the biotechnology company Genentech was to perform WGS on 23andMe consumers' samples, raising concerns about informed consent, data privacy, management of incidental findings and availability of the data to other researchers (Adam and Friedman, 2015). Although the ethical and legal study of DTC GT companies has been ongoing for almost a decade, it would appear that some of the ethical concerns about these companies and their research activities have not been resolved, but rather amplified as new sequencing technologies are implemented. Meanwhile, one of the DTC GT companies, 23andMe, has been remarkably successful in recruiting research participants (http://www.forbes.com/sites/matthewherper/2015/10/14/23andme-prepares-a-comeback-raising-115-million-at-a-1-1-billion-valuation/), thus gaining a significant share of the general community of biobank research and in doing so, potentially influencing the public perception of research. Noncompliance with ethical standards or recommendations by well-known companies could have significant negative implications for biomedical research in general. Therefore, it is particularly important to examine the behaviour of DTC GT companies and to promote the awareness and adherence to the ethical standards currently accepted and/or aspired to by the research community. In order to achieve this, it would be constructive to have the community of commercial companies weigh in on the development of best practice guidelines for the commercial realm along with relevant stakeholders such as consumers, patients and health care professionals.

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