Direct-to-consumer genetic testing

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Abstract

Introduction
Major advances in genetics have led to the identification of more than 1000 sequence variations that show an association with an increased risk of numerous complex diseases. These findings have led to valorisation initiatives such as the direct-to-consumer-genetic testing companies. Direct-to-consumer-companies provide individuals information about their genetic blueprint without necessarily involving healthcare professionals. Direct-to-consumer-genetic testing companies received a great deal of attention, however, the potential harms and benefits are under discussion. This study provides an overview of the current debate and the currently available direct-to-consumer-genetic testing services.

Conclusion
The amount of direct-to-consumer-genetic testing services, offering a wide variety of genetic tests, that have emerged in the past few years and the many discussions raised on the topic of direct-to-consumer-genetic testing among scientists and policy makers clearly highlights the growing popularity of such genetic tests.

Introduction
The field of genetics has become one of the most rapidly growing areas in biomedical sciences. In recent decades, major advances have been made through the discovery of more than 1000 sequence variations with statistically significant associations to numerous major complex diseases. Utilisation of this knowledge has been greatly facilitated through the development of cost-effective DNA sequencing technologies. Although decoding the first human genome took years and several billion dollars to complete, it is now possible to sequence an entire genome within about two weeks for less than 5000 dollars. Moreover, by the end of the year, it is expected that whole genome sequencing (WGS) will be available at a cost of $1000 or less.

These discoveries in the field of genetics, combined with a growing number of information-seeking individuals, have led to the development of direct-to-consumer (DTC) genetics. This is considered to be one of the greatest inventions of the twenty-first century, attracting powerful investors such as Google Ventures. Many commercial companies, mostly operating from the USA, currently offer DTC-genetic testing services directly to consumers, without necessarily involving a general practitioner or genetic counsellor.

Over the last couple of years, the emergence of DTC-genetic testing services has sparked significant attention from policy makers, public, healthcare providers, scientific researchers and the media. However, neither consensus nor research on DTC-genetic testing is available online via a secured website. Results of the genetic test are made available via a secured website (Figure 1).

Discussion

DTC-genetic testing services
Premise of DTC-genetic testing services
Genetic testing has come a long way since the first test was developed in 1963. At that point, genetic tests were only available through healthcare professionals; they ordered the appropriate test from a laboratory, collected and sent the samples, and interpreted the test results. However, due to the confluence of Internet and the completion of the human genome project, genetic tests have become publicly available. Via the Internet, consumers can now order genetic tests from genetic testing services without involvement of healthcare providers. After receiving the test, consumers are asked to collect a small DNA sample and send it back to the service. These services then extract the DNA and genotype it for hundreds of thousands to millions of genetic variants, with known disease susceptibility. After a few weeks, the results of the genetic test are made available online via a secured website (Figure 1).

The results provided by the DTC-genetic testing companies are typically reported as absolute risks, which is the probability that a specific individual will develop a disease during his lifetime. These absolute risks derive from odds ratio (OR) estimates and the population-based age-specific disease rates. OR estimates are based on information derived from genome-wide association studies and case-control literature on research in the field of DTC genetics. Lastly, we will briefly describe the efforts that currently have been made by policy makers to regulate DTC-genetic testing.
studies, designed to identify single nucleotide polymorphisms (SNPs) associated with a disease. SNPs are considered the most common variations within the structure of DNA. Using a multiplicative model, the ORs of independent SNPs are combined to estimate a person’s overall genetic risk of disease. By multiplying this with population-based age-specific disease rates, DTC companies can supply information about a person’s absolute risk of disease.

Emergence of companies
In 2007, deCODEme and 23andMe were first in offering and advertising multiplex genetic testing (i.e. genetic testing for several different conditions in a single testing session) directly to the public. Consumers could have their DNA genotype for over 500 000 SNPs at a price of approximately $1000, and information was provided on both susceptibility to diseases and ancestry. One year later, a third company, Navigenics, entered the DTC-genetic testing market, focusing on disease-related genetic risks only. For a price of $2500, they offered genetic testing on disease-risk with additional access to genetic counselling by telephone. Since then, the number of DTC-genetic testing companies has increased exponentially and prices have fallen dramatically. Moreover, ‘whole genomic sequencing’ has also become publically available. In 2009, Illumina, the market leader in providing DNA sequencing instruments, launched its own personal whole-genome sequencing service. Furthermore, 23andMe announced a pilot project in September 2011, aimed at providing raw exome data to its customers, for a price of $999.

Currently, over 30 DTC-genetic testing services are available offering health-related genetic testing. These companies vary widely in their laboratory model, purpose of the test, DNA collection method, price and their involvement with healthcare providers in the testing process. Table 1 shows 31 currently (March 2013) available DTC-genetic testing services offering health-related genetic tests, and provides information on their model of operation according to information received from their website. Companies exclusively offering paternity, genealogy or ancestry tests are not included.

Laboratory model
A wide range of technologies is available for DNA analyses. These can be classified into: (a) single-gene testing, (b) SNP-chip testing and (c) WGS. Single-gene and single-SNP testing provide information on a specific trait or disease. As this type of testing is less complex, cheaper and less time-consuming compared to the other types of testing, it is mostly used by small DTC-genetic testing services, such as CyGene Direct, DNA-Cardiocheck, DNA Dimensions, Graceful Earth, Pediatrix Medical Group, Psysomics. However, currently, the largest DTC-genetic testing service (i.e. 23andMe) offers whole genome SNP-chip testing. These chips make it possible to test

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for $10^5$–$10^6$ SNPs simultaneously, with relatively low resources. By carefully selecting SNPs associated with disease susceptibility, SNP-chip methods and associated analyses can provide a thorough assessment of risks for common and rare diseases.

WGS is currently only offered by two DTC-genetic testing companies, namely Knome and Illumina (WGS offered by Inneova in association with Knome). WGS determines the exact order of the three billion bases that make up the human DNA and, therefore, yields significantly more data than SNP-chips. However, since the ability to interpret this wealth of genetic data is currently limited, the immediate return in terms of medical relevance equals the information that is derived from SNP-chips.

**Purpose of tests**

The overall purpose of genetic tests performed by DTC-genetic testing companies given in Table 1 is to provide individuals with information about their risk of developing a disease. However, there is a great variety in what they offer. While some single-gene testing companies, such as Graceful Earth, Psynomics, Pediatrix Medical Group, DNA-Cardiocheck and Enterolab provide information on one particular disease (i.e. Alzheimer’s (AD), psychiatric disease, hearing loss, cardiac disease and celiac disease, respectively), the majority of currently available DTC-genetic testing companies test for a wide variety of diseases.

In addition to testing for disease susceptibility, most companies also reveal information on other categories such as (a) drug response (i.e. Psysomics, Pathway Genomics, GenePlanet, 23andMe, DNA testing of Canada, Genetic Center, Genetic Health, Kimball Genetics and Matrix Genomics); (b) ancestry (GenoType, Lumigenix, Genomic Express, Gene-Planet, easyDNA, N/A Dimension, 23andMe, DNA testing of Canada and Test Country); (d) paternity (Viaguard, easyDNA, N/A Dimensions, DNA testing of Canada and Test Country); (e) athletic ability (Gonio, CyGene Direct and Genomic Express) and (f) foetal gender testing (Viaguard, easyDNA, DNA Dimensions and DNA testing of Canada).

**DNA collection model**

Most DTC-genetic testing services (18 out of 33) ask consumers to collect a small sample of DNA by collecting buccal cells from the inside of the cheek. Another frequently used method is to collect saliva (18%). For this, consumers are asked to spit in a specially designed tube or container, pre-filled with adapted DNA stabiliser. In addition to these easy-to-use and non-invasive DNA collection methods, there are a few companies that use an invasive method to collect DNA by asking their consumers to visit a health clinic to have blood drawn (i.e. Illumina and Knome). However, although this method of DNA collection is invasive and might be less appealing to some consumers, the chance of receiving high-quality DNA is much higher compared to both saliva and buccal cell collection, particularly when subjects do not closely follow the instructions.

**Price**

There is a great variety in costs of genetic testing, depending on the type of test performed and the institution performing the tests. Overall, the costs of genetic testing increase with the number of diseases/mutations tested for. Consumers can purchase a single-gene test for less than hundred dollars, while the price for a whole genome scan can go up to several thousand dollars. However, similar services can vary widely in price depending on the company offering the test. For example, 23andMe charges $99 for their full scan (i.e. disease susceptibility, drug response, nutritional and metabolic characteristics, individual characteristics, ancestry), which is considerably cheaper than a comparable service performed by Gonidio ($1100). To justify their price, the latter company claims to offer a higher quality DNA genotyping techniques and reports on mutations 23andMe does not.

**Involvement of healthcare providers**

DTC-genetic testing services were first initiated to offer genetic testing outside of the healthcare system. Individuals ordered a genetic test online and were provided with their genetic test results without any involvement of professional healthcare providers. However, since offering genetic testing without the involvement of healthcare providers raised concern among opponents of DTC-genetic testing, this model of provision is changing. At first, consumers were allowed to order online without the approval of their doctor; some companies now require that a physician order the test (Illumina, Inneova, Knome, Pathway Genomics, Pediatrix Medical Group, Perkin Elmer Genetics and Psynomics). The same goes for providing test results. Although most of the DTC-genetic testing services still provide results directly to the consumer, they now actively encourage consumers to seek the advice of health professionals. A small number of companies offer consultation or genetic counselling as a part of their service (DNA Dimension, DNA testing of Canada, Genetic Health, Genomic Express, Gonidio, Inherent Health, Kimball Genetics, Knome, Pathway Genomics and VuGene) or at additional costs (23andMe, The Genetic Testing Laboratories and Test Country).
Advantages and disadvantages of DTC-genetic testing

With the increased public availability and low cost of DTC-genetic testing, it is important to formulate a balanced understanding of both advantages and limitations of the DTC-genetic testing services.

Advantages

The success of DTC-genetic testing is based on the assumption that the identification of increased genetic disease risk would directly influence risk-reduction behaviour. With the knowledge of an increased genetic risk of diseases, individuals can make proactive decisions about their health by choosing a particular diet, dietary supplement, lifestyle change or treatment to actively prevent diseases. With respect to the increasing prevalence of chronic diseases, this could be of a great advantage in the near future. This might result in a healthier population and reduce public healthcare costs.

Besides the potential, but as yet largely unproven (further elaborated in the paragraph 'Effect of DTC-genetic testing'), beneficial effect of genetic testing in terms of choosing risk-reduced behaviours, it has been argued that genetic testing also has a positive effect on preventive screening. In recent meta-analyses it has been shown that individuals with a known increased genetic disease risk are more willing to undergo preventive screening compared to individuals unaware of their genetic disease risk (for more details, see section 'Effect of DTC-genetic testing'). In this way, preventable diseases could be prevented effectively by early detection and application of appropriate behavioural or medical intervention. Furthermore, genetic testing could help in diagnosing disease caused by vague symptoms, as is, for example, the case with 'Celiac disease'. Celiac disease is a disease caused by an abnormal immune response to wheat gluten and similar proteins in barley and rye. Early diagnosis and treatment are important in this disease, because associated complications are of serious health threat and often irreversible unless the disease is treated. However, many of the symptoms causing celiac disease are similar to those experienced with several other health conditions. Therefore, most people who have this disease are unaware of it. Since genetics is the strongest risk factor for the development of celiac disease, genetic testing could be an effective tool in diagnosing celiac disease in an early stage.

Personalised medicine is another area that may potentially benefit from DTC-genetic testing. Knowledge of an individual's genetic susceptibility to drugs enables physicians to optimise their drug selection and dosing. Especially in an era where prevalence rates of comorbid conditions are climbing this could be highly beneficial in terms of medication choice, medication tapering and avoidance of unwanted side-effects in comorbid patients. Furthermore, it might lead to an increase in patient's compliance with medication, as it ensures safe and effective therapy. Also in terms of decreasing medical costs personalised medicine could be beneficial, since Beijer and Blaeij showed in an extensive meta-analysis that 16.6% of the total hospital admissions among elderly are due to adverse drug reactions.

Finally, a great positive effect of DTC-genetic testing is the promotion of patient autonomy and empowerment. In recent years, there has been a change in the role of a patient within health advocacy. Traditionally, patients have relied on doctors and conventional medicine. However, it is now becoming more important for a patient to play a more proactive role. Patients must become empowered and learn how to change health behaviours in order to obtain the best possible healthcare. Genetic test results may increase this feeling of empowerment and allow patients to discuss their care with their general practitioner. Furthermore, patients and their families may develop an increased awareness of the importance of family history.

Disadvantages

Because of all the mentioned potential beneficial effects of DTC-genetic testing, it may sound appealing. However, several disadvantages are attached to DTC-genetic testing in its current form.

A primary limitation of DTC-genetic testing services is the accuracy and adequacy of the risk information provided by the company. As mentioned previously, the currently most popular DTC-genetic testing services make use of the so-called SNP-chip. This technique is also used by academic researchers performing large-scale genome-wide association studies, and is shown to have an excellent analytical validity. However, small sampling errors or poor quality control could greatly affect its test performance, leading to genotypic misclassifications. In turn, this misclassification may lead to inaccurate risk estimates. As a result individuals might initiate unwanted behaviour changes, unnecessary anxiety and misuse of pharmaceutical medicine.

The observed inconsistency in risk information provided across DTC-genetic testing services has also raised questions about the accuracy and adequacy of the provided test results. For example, Imai et al. showed that the relative risk estimates for age-related macular degeneration ranged from 1.10 to 1.61 across three (i.e. deCODEme, 23andMe, Navigenics) DTC-genetic testing services. Moreover, for rheumatoid arthritis and atrial fibrillation both a protective and deleterious effect of the genotype on disease risk have been shown.
was indicated (range: rheumatoid arthritis, 0.90–1.85; atrial fibrillation, 0.80–1.80). This observed discrepancy in risk estimates between the different DTC-genetic testing services is explained by three factors: first, as each company has its own criteria for selecting underlying research, they might (a) evaluate different SNPs or (b) use different OR estimates for the same SNP. Second, different companies may choose different studies to obtain lifetime risk averages for the underlying populations. Third, the statistical methods to estimate the disease risk may also differ between the different companies. Generally a multiplicative model is used when combining different SNPs in diseases caused by multiple genes. However, the timing of conversion for OR to risk compared to the general population and the assumptions made about controls could vary among the DTC-companies.

A last concern regarding the accuracy of the genetic test results are the discrepancies observed between the results and the actual medical condition and family history of a consumer. The United States Government Accountability Office showed the genetic test results, provided by DTC-genetic testing services, of four out of five tested individuals conflicted with their factual medical condition or family history.

A second limitation of DTC-genetic testing services is that results might be misleading for consumers. Although there is evidence that high-educated individuals more often make use of genetic testing compared to low-educated individuals, the comprehension level of most consumers might be insufficient to correctly understand and interpret genetic test results. In this regard, the lack of genetic and statistical literacy of most of the consumers might be of great concern. Genetic literacy refers to an individual’s basic knowledge about genetics. In general, individuals know that genes affect their health status; however, a complete failure exists in terms of understanding how genes do so. Another common misinterpretation made by consumers is that they falsely interpret genetic information as deterministic. In this sense, individuals could increase their risk behaviour with the knowledge that they do not carry a certain genetic-risk variant or might evaluate risk estimates with a bias for certain diseases over others (e.g. due to personal experiences). In an alternative scenario, a carrier of a genetic-risk variant might develop negative psychological responses or experience anxiety. Deterministic interpretation of genetic test results may result in demotivation to change at-risk behaviour, since it might influence an individual’s beliefs on its current behaviour (will changing my behaviour reduce my disease risk?) and their ability to change their behaviour. In this regard, carriers of a certain genetic-risk variance might weaken their belief in that changing behaviour will reduce risks or in their ability to change behaviour, for example among smokers who learned that they have a genetic vulnerability to nicotine addiction.

Furthermore, since most DTC-genetic testing services only provide probability estimates, the level of consumer understanding with respect to the actual values of test results might be another concern. In the general population, individuals have been shown to have a relatively low skill level in comprehending, using and attaching meaning to numbers. Therefore, it may not be reasonable for DTC-genetic service providers to assume a consumer has the necessary knowledge to understand and apply their personal test results. Moreover, DNA-based disease risk estimates are less understood than other types of risk estimates.

Other concerns include: (a) the limited value of the test results given the low predictive ability of most diseases, determined by both the heritability and complexity of the disease. Current heritability estimates for most of the common chronic diseases indicate the importance of environmental factors in the development of these diseases. Since DTC-genetic testing services do not take environmental factors into account when predicting disease risks, consumers might receive inaccurate risks estimates. Moreover, most of the yet identified genetic variants only account for a small fraction of the genetic variance in diseases, and often a complex interplay of many different low-risk genetic variations are the cause of a disease.

(b) A lack of clinical utility (Burke, 2009 #77–Eng, #78). Clinical utility refers to the likelihood that the test will lead to an improved outcome. Since several diseases identified by DTC-genetic testing services lack established cure or prevention strategies, opponents criticise that information on these diseases should not be returned to the consumers.

Finally, some critics assert that DTC-genetic testing may lead to genetic discrimination, which may lead to social stigmatisation and/or create economic hardship, when results are used by insurance carriers or employers. Based on genetic knowledge of increased disease risks, health insurance companies might exclude groups from coverage or charge them higher rates. For example, insurances might ask higher premiums to smokers knowing they are at also carriers for gene-variation associated with increased risk of lung cancer. So far already a few insurance discrimination are documented and, in the UK individuals harbouring the BRCA mutation already pay higher lifetime insurance premiums that non-carriers.
Effect of DTC-genetic testing

Despite the great amount of attention received by DTC-genetic testing services from both opponents and advocates, there is a lack of empirical evidence supporting or refuting their notions. To date, a limited number of studies are available on the behavioural response to testing for single-gene conditions, and only three large prospective cohort studies are currently establishing the effect of multiplex genetic testing on consumer behaviour.

Research on single-gene genetic testing

Most of the studies examining how personalised genetic testing influences behaviour focused on one of the most important behavioural causes of death: smoking. Today, at least six randomised clinical trials and observational studies have established the impact of genetic information on smoking cessation, but conflicting results have been reported. Whereas the earliest studies showed no effect of genetic testing on smoking cessation, one more recent study has shown an increase in smoking cessation among those identified with an increased genetic susceptibility to smoking-related diseases.

Furthermore, a recent meta-analysis, including six studies with a total number of 3000 participants, also showed that an identified increased genetic susceptibility to smoking-related diseases had a motivational effect on smoking cessation, in that it resulted in a higher risk perception and more motivation to quit smoking. However, an earlier meta-analysis on the effect of single-gene testing and risk-reducing behaviour and motivation to undertake such behaviour did not show significant evidence of a beneficial effect on both short-term (less than six months) and long-term (after six months) smoking cessation.

The effect of single-genetic testing on screening behaviour has also been an important question of research in the past years, especially regarding the most frequently occurring types of cancer—breast cancer, ovarian cancer and colon cancer. A systematic review showed that the overall effect of genetic testing on screening behaviour was positive. For example, for breast cancer it was shown that the overall compliance with screening was high and consistent across 14 studies. Carriers of the BRCA1/2 gene variants, which are associated with an 40%–60% increased risk of breast cancer, were more likely to undergo preventive screening compared to non-carriers. The same positive screening behaviour change was observed for ovarian cancer as well as for colorectal cancer. Similar results were shown in a more recent systematic review, including 16 studies on breast and ovarian cancer; 11 studies on colorectal cancer and one on both breast and ovarian and colorectal cancer. Again, carriers of gene variants associated with an increased risk of either breast and ovarian cancer or colorectal cancer were more likely to make use of preventive screening than non-carriers.

Only a very limited number of studies have evaluated the effect of single-gene testing on behaviours such as diet, physical exercise and use of medication or vitamins. In this area, the REVEAL study has been the most cited. Within this study, adult children of individuals with AD were offered testing for the apolipoprotein epsilon 4 genotype, which confers susceptibility to AD. The authors showed that knowing genetic information about AD significantly increased positive behaviour changes with respect to diet, physical exercise and medication/vitamin intake. To our knowledge, only one other study, till date, has assessed dietary behaviour as an outcome. Individuals genetically identified with hypercholesterolaemia showed a greater tendency to eat a low-fat diet. In the same study, physical exercise and medication use was also assessed, both showing positive changes in response to genetic susceptibility to hypercholesterolaemia. Other studies investigating the effect of genetic testing on diet and physical exercise focused on an individual’s motivation to change their dietary and physical activity behaviour. Frosch showed that individuals with an increased genetic susceptibility to obesity had a greater intention to eat a healthy diet compared to individuals with an average risk to obesity. In line with this result, Hicken et also showed that individuals genetically identified with the fictitious ‘Asch syndrome’ demonstrated a positive change in dietary behaviour.

Research on multiplex genetic testing

To answer the question that arose from genetic testing, ‘Can multiplex genetic testing lead to prevention of diseases, by inducing positive behaviour changes?’ three large prospective cohort studies were recently initiated. Here, we will briefly describe each of them.

The ‘Multiplex Initiative’ was the first study initiated to answer questions regarding genetic testing. This study was launched in 2006 with the main goals of gaining information from a population-based sample of adults about who, when offered genetic susceptibility testing for common health conditions, would be interested in being tested and to explore behavioural responses to test results among those who opted for testing. Recruitment for the Multiplex Initiative began early in 2007 and is currently still ongoing. At the end of the recruitment phase, approximately 1500 individuals will be included to undergo a multiplex genetic test for 15 different genes associated with a slightly increased risk for common health conditions. An early report showed...
that patients were unlikely to interpret genetic results as deterministic of health outcomes\textsuperscript{69}, suggesting that it is unlikely that patients would develop negative psychological responses with the knowledge of carrying a certain genetic-risk variant.

A second, and still ongoing, study has been initiated by researches from the Coriell Institute for Medical Research (Camden, New Jersey, USA) under the name 'The Coriell Personalised Medicine Collaborative'. Their aim is to answer the question 'Can personalised genetic information be used to improve people's health?' Ten thousand volunteers will be included, all who will submit a small saliva sample for genome analysis and answer online health questionnaires about family history, lifestyle and personal medical history\textsuperscript{57}. As this study is still in an early phase, no data have been reported.

The most recent study initiated in the area of multiplex genetic testing research is the 'Scripps Genomic Health Initiative', which aims to enrol up to 10,000 subjects who will have their genomes tested by DTC-genetic testing services to assess how test results affect lifestyle decisions\textsuperscript{10}. Preliminary data did not show measurable changes in anxiety levels, dietary fat intake and physical exercise\textsuperscript{10}. Furthermore, no effect was observed on the use of screening. However, the number of screening test that subjects intended to complete with greater frequency was significantly increased after genetic testing.

In addition, the Harvard Medical School started the Personal Genome Project, which aims to investigate genetic and environmental contributions to human traits through open sharing of participants' genome sequences and personal information\textsuperscript{16}. The Personal Genome Project enrolls volunteers who are willing to share their genome sequence, and other personal information such as health and medical data with the scientific community and the general public. To date, already 2000 volunteers have signed up to have their genomes sequenced as part of this project.

Although the early promising results on the impact of single-genetic testing on positive behaviour changes and the growing body of literature on the impact of multiplex genetic testing on behaviour, there is currently no clear picture and a lot of work is still to be done within this field of research.

Regulation of DTC-genetic testing
Due to the increased popularity of genetic testing in the general public and the lack of consensus and empirical evidence on positive effect of DTC-genetic testing, it is important for policy makers to increase regulation in areas of test accuracy and adequacy, genetic counselling and accuracy of advertising in order to protect consumers. Therefore, several legislative efforts have been made to regulate DTC-genetic testing.

For example, in the USA, the Secretary’s Advisory Committee for Genetics Health and Society SACGHS was established in November 2004 to provide advice to the Secretary of Health and Human Services about the broad range of human health and societal issues raised by the development and use, as well as potential misuse, of genetic technologies. They advised to conduct an analysis of the public health impact of DTC advertising and direct access to genetic tests\textsuperscript{59}. As a response, an assessment of the scientific accuracy of claims made by companies advertising genetic tests on the Internet was initiated by relevant federal agencies as well as an evaluation of the public health impact of DTC marketing of genetic test\textsuperscript{59}.

In 2006 the Food and Drug Administration (FDA), which has the authority to regulate medical devices, and the Centre for Disease Control and Prevention, which promotes health and quality of life, reported to the Federal Trade Commission that some genetic tests lack scientific validity, and others provide medical results that are meaningful only in the context of a full medical evaluation\textsuperscript{61}. One year later, when multiplex genetic testing became publicly available, the FDA started to meet with companies proving these tests in order to better understand what they were in fact doing or planning to do. In 2010, the FDA sent a letter to the DTC-genetic testing service called 'Pathway genomics corporation' saying ‘that their offer appeared to meet the definition of a medical device as that term is defined under the FDA, and clearance or approval by the Agency was necessary in order for them to market their product’. Following this letter, the Pathway genomic corporation stopped marketing directly to consumers. In the same year, the FDA sent the same letter to 19 more companies offering DTC-genetic testing and started to hold public meetings to begin dialogue with stakeholders concerning regulation of tests\textsuperscript{62}.

In addition, both the American Medical Association and the American Society for Human Genetics made recommendations to the federal government to improve regulation of DTC-genetic testing companies, regarding the accuracy of the information provided to consumers and the involvement of a professional healthcare provider\textsuperscript{63,64}. Furthermore, the U.S. Government Accountability Office was asked to investigate DTC-genetic tests on the market and the advertising methods used to sell these tests and cited ‘misleading test results’ and ‘deceptive marketing practices’\textsuperscript{29}.

Also in Europe, where DTC-genetic testing is only offered by a limited number of companies, this...
issue has been raised in many discussions at the government level. Already in 2002 the UK’s Human Genetics Commission hunted to distinguish between genetic tests with high, moderate and low impact. More recent, this commission issued standards in ‘the Common Framework of Principles’ on several aspects of DTC-genetic testing services, including the marketing of services, the laboratory analysis of biological samples and the level of support that the consumer should be provided with when purchasing and receiving genetic tests results in the hope they lead to the development of codes of practice for consumer-purchased genetic tests in Europe.

In 2003, the ‘European Group on Ethics in Science and New Technologies’ published a statement to decision makers of the implications of DTC-genetic tests. Furthermore, several other European organisations made recommendations to policy makers regarding the legislation of DTC-genetic testing, such as (a) the ‘European Society of Human Genetics’, who paid attention towards DTC-genetic testing and concluded that ‘DTC tests and the advertisement of genetic tests of unproven benefit or without adequate independent genetic counselling contradict with the professional standards the ESHG sustains’, (b) the ‘European Academies of Science’ and the ‘Federation of European Academies of Medicine’, who collaborated to develop reports in the hope they lead to the development of codes of practice for consumer-purchased genetic tests in Europe.

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The main aim of the project is to ensure that all aspects of genetic testing are of high quality thereby providing accurate and reliable results for the benefit of the patients, and (b) ‘Public Health Genomics European Network’, to serve as an ‘early detection unit’ for horizon scanning, fact findings and monitoring of the integration of genome-based knowledge into public health. This project already accomplished the initiated National task Forces on Public health genomics (i.e. the use of genomics information to benefit public health) in over 15 EU Member states and is currently developing European Best Practice Guidelines for Quality Assurance, Provision and Use of Genome-based Information and Technologies.

Currently the most important endeavour to provide regulations for DTC-genetic testing is the ‘Additional Protocol to the 1997 Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the application of Biology and Medicine, concerning Genetic Testing for Health Purposes’, published by the ‘Council of Europe’. This protocol includes rules and principles, among others, regarding the quality and clinical utility of the provided genetic tests, genetic counselling and data protection. As it documents guidance regulations in a rapidly evolving area of research it is not surprising that this guidance is regularly reviewed and updated.

Conclusion
The amount of DTC-genetic testing services, offering a wide variety of genetic tests, that have emerged in the past few years and the many discussions raised on the topic of DTC-genetic testing among scientists and policy makers clearly highlights the growing popularity of such genetic tests. The idea that DTC-genetic testing could help prevent the occurrence of many common chronic diseases by inducing positive behaviour changes seems phenomenal! Especially in a world that is facing a rapidly ageing population accompanied by a steeply increased number of people suffering from chronic disease. However, there is still little evidence to support these high hopes and several analytic, clinical and legal issues pose serious threats on this business. Therefore, before moving on to this relatively undiscovered area we should carefully consider the risks and yet-to-be-solved issues.

References
Review


