An epidemiologic-based survey of public attitudes towards predictive genetic testing in Russia

Many new genetic tests for common multifactorial disorders are becoming available to individuals, including direct-to-consumer genotyping services. Typically, studies of public attitudes reveal a high level of interest for individual genotyping. In a Russian urban population, 85% of 2000 respondents answered positively to a question about their own willingness to undergo predictive genetic testing for preventable health conditions. Gender, age and health status significantly influenced response. Multivariate discriminant analyses revealed that wanting to know about probable future diseases, readiness to improve lifestyles and an interest in learning about individual genome characteristics are the most important predictors for wanting to be tested. Along with the high level of interest, highly overestimated expectations were encountered in many studies. With the low predictive abilities of currently available genetic tests for common disorders, proper interpretation of the data and genetic counseling are essential. There is a need for prospective validation of genetic panels for risk assessments, and for efforts to measure the effects of genetic information disclosure and how this information might contribute to lifestyle changes.

KEYWORDS: common diseases ▪ direct-to-consumer genetic service ▪ genetic discrimination ▪ genetic risk assessment ▪ genetic testing ▪ predictive diagnostics ▪ preventable health condition ▪ public attitude

Oksana A Makeeva[†1,2*], Valentina V Markova[1*], Allen D Roses[3,4] & Valery P Puzyrev[1]

[1]Research Institute of Medical Genetics of the Siberian Branch of the Russian Academy of Medical Sciences, 10 Nab. Ushaiky, Tomsk 634050, Russia
[2]Research Institute of Complex Problems of Cardiovascular Diseases of the Siberian Branch of the Russian Academy of Medical Sciences, Kemerovo, Russia
[3]Deane Drug Discovery Institute, Durham, R David Thomas Executive Training Center, 1 Science Drive, Suite 342, Box 90344, Durham, NC 27708, USA
[4]Institute for Genome Sciences & Policy, Duke University, Durham, NC, USA
[†]Author for correspondence:
Tel.: +7 382 251 2228
Fax: +7 382 251 3744
oksana.makeeva@medgenetics.ru
[*]Authors contributed equally to the research

Genetic testing for common diseases has become one of the most controversial topics present in the recent genetics literature [1–6]. The business of providing reports of personal genetic interpretations to individuals fascinated with the idea of gaining information about themselves raises many concerns. The scientific and medical communities are faced with the reality of direct-to-consumer (DTC) genetic services becoming available before critical medical implications have been widely considered. This increases the threat of a 'culture war' between the genetics community, which may be motivated by excessive paternalism [7], and commercial venders of DTC who solicit genetic samples from the public for individual disease risk predictions. An initial wave of criticism and rejection of DTC genetic testing is gradually shifting toward greater tolerance and constructive discussions of regulatory oversight, the ethics of testing without defined subsequent medical care, and even practical recommendations on how to improve businesses [6–9]. Meanwhile, big DTC genetic companies are making an effort to address criticisms by launching long-term prospective studies to evaluate how genetic information can influence behaviors, by improving disease-specific risk assessment strategies and by implementing many of the recommendations provided by the research community [101–103].

For both oversight and promotion, it is essential to understand public opinions and expectations regarding individual genotyping and the factors that influence attitudes towards predisposition genetic testing. A very high level of interest and acceptance for predictive genetic testing, including susceptibility for common health conditions, has been reported by a number of studies [10–15,104]. This is partly a consequence of publicity about genetic research developments [16], which sometimes overestimate benefits such as prevention of a disease and underestimate potential harms, including psychological adverse outcomes and possible false-positive and false-negative results, leading to unneeded medical interventions or false reassurance.

A great part of our current understanding of attitude toward testing of disease susceptibilities has come from studies of individuals at risk of highly heritable disorders, for example, certain cancer syndromes and Alzheimer's disease. A unique aspect of such studies is that individuals from disease-burdened families already typically perceive themselves to be at increased risk and are typically encouraged to be tested [11,17–20]. There are very few population-based studies, published or in progress, that evaluate the effects of offering susceptibility testing to a large and demographically heterogeneous population. It is also likely that different viewpoints concerning

future medicine part of fsg

genetic testing of individuals exist in different countries, as public attitudes are under the influence of a broad spectrum of different socio-economic, political and historic peculiarities and traditions.

In this article, we comment on some of the important issues that have recently been raised, and also highlight some of the findings from a population-based study of a Russian urban population (2000 respondents) [21] and their attitudes to different aspects of genetic testing and disease-risk assessments.

Public interest in genetic testing for common diseases

A number of studies of public attitude towards genetic testing in general or with respect to specific diseases have been published thus far. Both population-based and disease-specific studies typically report a high level of acceptance and interest in personal genetic testing. For example, one of the most important findings from our population-based survey of 2000 respondents in Russia was a highly positive response to a question about risk assessment for avoidable diseases: 85% of surveyed people gave an affirmative answer to the question: "Would you like to estimate the genetic risk for diseases that are avoidable through preventative measures?" [21]. A rephrased question, where genetic testing was not mentioned nor was there mention of a disease to be prevented ("Would you like to know about probable future diseases?") gave significantly fewer positive answers – 68%. Women said they would opt for testing more often than men, and people who reported their health as 'excellent' were usually less interested in risk assessment. In addition, the younger the age group studied, the higher the proportion of subjects who wanted to undergo genetic testing. Neither marital status nor education level influenced the answers to these questions.

This positive response has been noted in other populations, when questions about genetic testing in general were asked, or when the questions concerned risk of specific diseases. In addition, population-based studies of public attitudes to common disorders have also reported a predominantly positive attitude toward genetic testing, regardless of the methodology used (telephone survey, postal interrogation, internet or focus group study):

- A high rate of acceptance of genetic testing was revealed in a Finnish population (n = 1169): approximately 90% agreed that genetic testing should be available to everyone who wants to know whether he or she carries disease genes [12,14];
- In a representative German sample (n = 2076), 59% agreed with the statement: "Genetic testing should be available to anybody who wishes to have information about her/his disease" [11];
- An internet survey of a representative sample of UK residents (n = 2510) revealed that the majority (81%) would consider genetic testing if it was offered by their doctor [105];
- A survey of a representative sample of the European public (~6,000 people from six countries participated), conducted to determine attitudes towards genetic testing for personalized nutrition, revealed that two-thirds of respondents reported they would be willing to undergo genetic testing for personalizing their diets [22];
- In a telephone survey conducted in a representative US population sample, 79% of respondents stated that they would take a hypothetical genetic test to predict their risk of developing Alzheimer's disease in the future [20];
- In British population survey, 69% of people expressed their interest in being tested for genetic susceptibility to heart disease, and 64% expressed interest in susceptibility to cancer [10];
- A focus group study of public attitudes towards genetic risk prediction of psychiatric diseases showed that 24 out of 36 participants indicated interest in taking a genetic test for susceptibility to major depression, if it was available [15].

Surveys of people from families with inherited disorders and cancer syndromes showed that most people who perceive themselves at increased risk have a strong desire to be tested and to test their children for mutation carriership.

- A study, conducted in the USA, of a sample of parents with normal hearing who had deaf children revealed that 96% of parents expressed approval for genetic testing for deafness and 76% stated that they were interested in being testing themselves [17];
- Most parents (87%) from families with familial hypercholesterolaemia wanted their children to undergo a genetic test for mutation carriership (The Netherlands, 2002) [18];

- In a German study, as much as 100% of persons who are themselves at risk of a hereditary disease (hereditary nonpolyposis colorectal cancer/familial adenomatous polyposis) agreed to that statement: "Genetic testing should be available to anybody who wishes to have information about her/his disease" [11];
- A comprehensive review of surveys of gene testing for breast cancer was conducted by Elwood [19]. Most of the reviewed studies reached similar conclusions: approximately 80–90% of women who were unaffected, first-degree relatives of patients with breast or ovarian cancer stated they wanted to be tested. Interest in testing was positively related to perceived risk in many of the cited studies;
- A study by Meiser and co-authors assessed the interest of people from families with multiple cases of bipolar disorder for testing for gene variations associated with the disease. Interest in genetic testing ranged from 77 to 92% and uptake of genetic testing was positively associated with the degree of certainty with which any test would indicate the development of a disease [23].

It should be mentioned that the high level of interest in testing expressed in surveys may not always translate to real demand for genetic testing. Studies of first-degree relatives of breast cancer patients demonstrated that, while over 80% of the study participants gave affirmative answers to questions on wanting to be tested, only 50% actually gave blood samples for testing [24]. Even with Huntington's disease, where mutation analysis is greater then 99% sensitive, one study demonstrated that at the time of the first counseling session, almost three-quarters of counselees wanted to be tested; however, over the 11 years of the investigation, only 52% of persons at risk actually obtained genetic test results [25]. In Canada, between 1987 and 2000, as few as approximately 18% of the population estimated to be at risk of Huntington's disease obtained a genetic test for the disease [26]. It is likely that the uptake of genetic testing for low-risk alleles related to common, multifactorial diseases will be lower than for testing for high-penetrance gene mutations for inherited disorders [23].

However, the high level of public interest in genetic risk assessment that is currently seen will probably promote the growth of commercial genotyping services, including DTC genotyping. Many studies also note that lay people's expectations are too high [27–28]. These two important observations may have a serious impact on further developments in personal genotyping services.

Factors that influence people's decisions to undergo genetic testing for disease predisposition

Not much is known about factors that motivate individuals to be willing to undergo genetic susceptibility testing for common preventable health conditions. What is known predominantly comes from studies of individuals with a high lifetime risk of hereditary cancer syndromes or Alzheimer's disease, who are cognizant of and concerned about genetic risk [29]. Such studies provide a poor framework for understanding the motivations of healthy people to be genotyped in order to assess susceptibility for common diseases for which genetic variants confer relatively small increases in risks. Anxiety about health cannot be the only reason that drives people to genotyping to estimate common disease risks. Gurwitz and Bregman–Eschet suggested that early users of personal genomics services may be "motivated by intellectual curiosity" rather then being driven by a deep concern about their future health [6].

In our survey of a Russian population, we attempted to identify the factors that determined whether people would take a genetic test. Several possible reasons were evaluated and rated according to the frequency of response to a host of survey questions [21]. In order of importance, the motives that most influenced people were:

- Anxiety about health (38% of all answers);
- Doctor's recommendation (23%);
- Availability of more detailed data (18%);
- Curiosity (17%);
- Family's or friend's advice (4%).

Several characteristics affected response: women are more anxious about health than men (43% of women offered this as a reason for testing vs 30% of men), while men mentioned curiosity more often than women did (20 vs 15%). In the oldest age group (≥65 years), the most frequently given reason for undergoing genetic testing was a doctor's recommendation (52% vs 21–23% in all other age groups). Curiosity as a motive for testing decreased with age (from 20% in the youngest to 13% in the oldest group) [21].

Reasons to reject testing were distributed in the following order:

- "Lack of money to pay for testing and possible treatments" (41% of all responses);
- "Lack of time" (20% of all responses);
- "Nothing" (18%);
- "Fear of discovering predisposition to a disease" (14%);
- "Fear of possible treatment" (4%);
- "Genetic testing is useless" (3%).

People in the oldest age group differed significantly from other groups in their response, as 22% indicated that they thought that, "testing is useless" compared with only 2–4% in all other age groups. Fear of discovering a predisposition to a disease slightly correlated with the level of education of the respondent: the higher the education level, the less this reason was given for unwillingness to be tested [21].

Data from this Russian study support the notion that anxiety about health is the primary motivator for undergoing genetic testing for common health conditions, but curiosity is also important factor. Furthermore, a large component of Russian society relies on doctors' recommendations. Not surprisingly, the price of testing is one of the major constraints for seeking commercial genotyping. New technical achievements leading to reduction of financial barriers will probably result in considerable market growth.

In other studies, it has also been shown that age, gender, level of education, genetics knowledge and awareness of a disease influence people's interest in undergoing predictive genetic testing, but the factors, or relative importance of the factors, may differ from country to country [11–14]. Inconsistent with some other studies [12–13], the Russian study indicated that women are more supportive of personal genotyping and disease risk assessments compared with men. People with poor health or of a younger age are more likely to opt for testing. However, in Russia, the respondent's educational level and marital status have no measurable effects [21].

The attitude toward different aspects of genetic testing, such as a fear of genetic discrimination and concerns about post-testing lifestyle changes, may affect people's decisions about undergoing genotyping. In our study of a Russian population, multivariate discriminant analysis was used to determine the personal characteristics and beliefs, obtained from the questionnaire, which most influenced the expressed desire to either take or not take a predictive genetic test. Responses to the questions about people's beliefs in the usefulness of genetic testing, the availability and promotion of testing, attitudes to prenatal genetic testing and testing for pregnant women, perception of the threat of genetic discrimination, opinion about impact of testing on lifestyle changes, and demographic and social characteristics were analyzed (**Box 1 & Table 1** present survey items that were analyzed with respect to the willingness to take a test for avoidable diseases). The predictive ability of each of the proposed models was determined by the fraction of respondents who were correctly classified into group.

Several discriminant models were tested. The model that best predicted willingness to undergo predictive genetic testing was composed of three variables – answers to questions 2, 3 and 4 (characteristics of the discriminate function are presented in **Table 2**). This model correctly classified supporters of genetic testing 91% of the time and correctly identified those who would not take a test 67% of the time (total correct classification was 88%) (**Table 3**).

The results indicated that the best predictors of acceptance of proffered genetic testing were affirmative answers to the questions:

- "Would you like to know about probable future disease?"
- "Would you try to change your lifestyle ... if a high risk of disease were identified?"
- 'Would you like to know more about your personal genome?"

A large, population-based study that evaluated the effects of offering testing for multiple common health conditions had shown that individuals who sought genetic testing were among those who were most motivated to take steps towards healthier lifestyles [29]. Similarly, in our study, a positive answer to a question about willingness to make lifestyle corrections was one of the three most important variables for predicting who would take a predictive genetic test.

Possible risks & harms of predictive genetic testing

It has been widely discussed in the literature that genetic risk prediction can result in serious psychological outcomes, such as increased distress, anxiety and stigmatization of tested people [30]. Several studies have demonstrated that

people who are worried about their loss of privacy and the risk of discrimination are less likely to accept predictive genetic testing [15,31,104].

In our survey, 48% of respondents reported that they "believe that if genetic testing results become publicly available, they could result in the discrimination of tested people". More men then women had concerns about discrimination, and people with poor health status expressed their concerns more often compared with those with 'good' or 'excellent' health. Age, education, family status and other measured characteristics did not influence the response to this question.

A survey of 1119 people in USA (carried out in 2007) revealed that while the majority supported genetic testing for research and healthcare, 92% of surveyed people also expressed concerns that if the results of a genetic test suggested increased risk for a disease such as cancer, the information could be used in ways that were harmful to the tested individual [104].

Although there were many early presumptions and discussions about possible unfavorable outcomes of predictive genetic testing, a review of recent publications indicated that psychological or behavioral harms were not as serious as was assumed [30,32]. Several studies found little psychological impact (or harm), or that negative effects on those who have been tested were short-lived [30–34]. Anxiety may be considerably diminished with proper pre- and post-testing counseling [30]. A recent study by Green and co-authors examined the effect of disclosing *APOE* genotype to asymptomatic adults with a family history of Alzheimer's disease, measuring symptoms of anxiety, depression and test-related distress [34]. They found that disclosure of *APOE* genotyping results did not present a significant short-term (6 weeks, 6 months or 1 year) psychological risk and that test-related distress was reduced in *APOE* ε4-negative

Box 1. Demographic and social characteristics that were analyzed by multivariate discriminant analysis in respect to target question about genetic risk assessment for preventable diseases.

- Self-assessed health status
- Gender
- Age group
- Education level
- Professional employment
- Marital status
- Average income for one family member

Table 1. Questionnaire items that were analyzed by multivariate discriminant analysis in respect to target questions about genetic risk assessment for preventable diseases (question 1)†.

Question	Frequency of response (%)		
	Yes	*No*	*No response*
1. Would you like to estimate the genetic risk for diseases which are avoidable through preventative measures?	85.2	14.8	
2. I would like to know about probable future diseases	68.3	31.0	0.7
3. Would you try to change your lifestyle: to give up bad habits and to follow a recommended diet or take medications if a high risk of disease were identified?	88.5	11.5	
4. I would like to know more about my genome (the entire genetic information)	82.2	16.8	1.0
5. Knowing genetic mechanisms of diseases will help people to live longer	81.3	16.8	2.0
6. Knowing their own genetic variants allows people to control their lifestyle easier	81.4	17.2	1.4
7. If people know their genetic background, they would tend to shift the blame for their diseases on it	56.0	42.0	2.0
8. If people know their genetic background, it influences their self-assertion	61.8	36.8	1.4
9. Genetic testing results can limit people in their choice of lifestyle	38.8	59.8	1.4
10. Genetic tests should be promoted extensively	68.6	28.2	3.2
11. I believe it is essential to assign more money for genetic developments	85.9	10.9	3.2
12. All pregnant women should be offered genetic testing	87.2	11.4	1.4
13. If serious genetic abnormalities have been discovered in a fetus, termination of the pregnancy can be recommended to a woman	78.0	18.5	3.5
14. I believe that genetic testing results, if they become publicly available, can result in discrimination of tested people	48.0	49.8	2.2
15. Genetic researches are beneficial	92.4	4.5	3.1
16. Do you know about any inherited disorders in your family?	31.6	68.4	
17. Would you like to know about your ancestry with the help of DNA research?	83.0	17.0	

†*Study design and procedure had previously been described in detail* [21]. *Survey participants (n = 2000) were residing in Tomsk, a city of 500,000 people in West Siberia, Russia. Most of the responders were contacted at their work places, enrolled through social/hobby associations and during annual preventive medical examination. A total of 10% of questionnaires were completed on the internet. Questionnaires obtained through the internet were compared with the forms collected in a usual way and did not differ in the frequency of completion. Nonresponse rate was less than 10%.*

Table 2. Results of the discriminant functional analysis for the model predicting answers to the questions about willingness to take a predictive genetic test for avoidable diseases.

Variables: answers to the questionnaire items	Step	Stepwise Wilks' λ	Partial λ	F-to-remove	p-value	Tolerance
1. I would like to know about probable future disease (yes/no)	1	0.749	0.909	199.23	<0.0001	0.895
2. Would you try to change your lifestyle: to give up bad habits and to follow a recommended diet or take medications if a high risk of disease were identified? (yes/no)	2	0.744	0.915	186.04	<0.0001	0.992
3. I would like to know more about my personal genome (the entire genetic information) (yes/no)	3	0.719	0.947	110.53	<0.0001	0.894

Wilks' λ: 0.681 approximately F (3.199) = 311.51; p < 0.00001.
Wilks' λ is used to test the significance of the discriminant function as a whole. The stepwise method selects the predictors that contribute most to the discrimination, and eliminates those that are not suitable for the analysis. Wilks' λ and the F-value for the change in Wilks' λ (F-to-remove) were evaluated. The more important the variable (demographic data or responses to questionnaire items) in classifying the grouping variable (pros and contra groups), the higher its stepwise Wilks' λ. Partial Wilks' λ also tests which characteristics contribute significantly to the discriminant function: the smaller the partial λ, the more that variable contributes to the discriminant function. Tolerance is the measure of redundancy of particular variable in the model: the lower the tolerance, the more redundant that variable is.

persons (where the ε4 allele is associated with increased risk) [34]. In an earlier study on attitudes about genetic testing for Alzheimer's disease, most respondents (79%) were prepared to learn whether they carried a gene for Alzheimer's disease, even though there are no preventive or curative treatments available [20]. Respondents stated that if they tested positive, they would take several important measures: a majority stated they would obtain advance directives, purchase long-term healthcare insurance and put their finances in order. These data suggested that people may have strong personal preferences for testing information. In this and many other studies, the strongest inclination for taking a genetic test was among those with a family history of the disease or experience caring for someone with the illness [11,17–18,20]. These data also suggested that more knowledge may increase the demand for testing.

However, more serious damage to health than psychological distress may ensue from genetic testing if unnecessary medical interventions are undertaken in response to incorrect test results, incomplete understanding or inappropriate interpretation. Testing of healthy people without assessing other risk factors (e.g., testing for breast cancer of women without a suggestive pedigree) can potentially cause serious harm (e.g., prophylactic mastectomy). It is a general rule that the more tests performed, the greater the chance of finding something that appears to be wrong and the risk of false-positive and false-negative results is also increased [106]. Either situation can lead to unnecessary treatment or incorrect reassurance. Most of the genome-based tests that are currently available are not designed for use by people without symptoms (for review of the reasons refer to [106]). A good example is prostate cancer: it has recently become policy to not offer screening for prostate cancer for individuals without symptoms, because prostate tumors commonly grow slowly and primarily affect elderly men. Its diagnosis often has no effect on life expectancy, but a positive test for prostate cancer can lead to dangerous treatment with medications, radiotherapy or surgery [106].

Although many studies identify a high level of interest in testing for common health conditions, the gap between expectations and reality can be wide. Many genetic test interpretations are based on very preliminary research and often have low sensitivity, specificity and predictive value – either positive or negative. Usually, the publicity surrounding genetic screening tests suggests benefits (prevention or mitigation of a disease) that are overestimated and the potential harms are not adequately conveyed. These factors result in unrealistic expectations from genetic testing, disappointment and sometimes unnecessary medical interventions [27–28]. The study of

Table 3. Classification table of correct estimates with the three variables (answers to questions 2–4 of Table 1) for the discriminant model, predicting response to the target question about personal genetic risk assessment.

Answers	Percentage of correct classification
Predicted classification for the group answered 'yes' to predictive testing	91.4
Predicted classification for the group rejected testing	67.3
Total of predicted classification	87.8

public attitudes about testing for Alzheimer's disease, mentioned earlier, found that 79% of a general population stated they would take a hypothetical genetic test to know whether they would eventually develop Alzheimer's disease. However, only 45% of respondents would take a 'partially predictive' genetic test that had a one in ten chance of being incorrect [20]. Even with the most replicated and validated susceptibility gene for any complex disease, *APOE* is only predictive of eventual Alzheimer's disease diagnosis for *APOE4* carriers who are already cognitively impaired [35]. Experts decided that even this test was not suitable for predicting disease risk in normal individuals [36]. All of the proposed genetic tests for complex diseases have lower predictive test capabilities for normal individuals than *APOE* does for Alzheimer's disease.

One study found that most women had a high level of interest in being tested for breast cancer susceptibility [28]. However, the scored interest was for a genetic test capability that did not yet exist (high positive predictive value followed by effective, noninvasive and preventive therapy). There was less interest in the less predictive tests that were actually available. The Alzheimer's disease and breast cancer examples suggest that people may be motivated to take a genetic test that will not lead to the disease prevention they are seeking. In these situations, careful counseling is required. This is a problem with internet-based testing that operates independently of effective consulting and medical services.

Conclusion

In conclusion, there is a very high level of interest in predisposition genetic testing in the general public. Anxiety about future health and the belief that behaviors can be modified in order to pursue healthier lifestyles are the most important reasons given by people for wanting to be tested. Several studies conclude that more knowledge about diseases can increase peoples' desire to learn about their own genetic predisposition to disease. People may perceive genetic information as valuable and important not only for health-related matters but with respect to other major life decisions. In conjunction with a high level of interest are highly overestimated expectations as the outcome of genetic testing may not lead to the desired medical outcomes. Inflated expectations can result in disappointment, and the genetic tests may sometimes lead to unnecessary medical interventions. With the low predictive abilities of currently available genetic tests for common diseases, proper genetic counseling before and after testing is essential. There is also an urgent need for prospective validation of proposed genetic panels for disease risk assessments and to study the effect of disclosure of genetic information on lifestyle changes. There are recent examples of both types of studies.

Currently, only a few genetic markers are prospectively validated. A study design for prospective validation of genetic markers to predict the age of onset of Alzheimer's disease has been proposed recently [37]. A poly-T repeat (rs10524523) in intron 6 of the *TOMM40* gene, identified by deep sequencing of the *APOE* linkage disequilibrium region combined with phylogenetical analysis of the sequences, is associated with the age of onset of Alzheimer's disease [38]. This genetic variant will be validated in a pharmacogenetically assisted prevention clinical trial, Opportunity for the Prevention of Alzheimer's disease (OPAL). Healthy individuals between 62 and 87 years of age will be prospectively segmented into groups based on genotype and age. The groups propose to stratify subjects with high and low risk of developing cognitive impairment or Alzheimer's disease within the next 5–7 years. Validation of the predictive ability (positive and negative) of a genetic panel consisting of the *TOMM40* rs10524523 and *APOE* variants will be accomplished in the same clinical trial conducted to test the efficacy of a drug for delay of onset of Alzheimer's disease. This study design allows for simultaneous validation and efficacy testing within a 5-year period. Prediction of disease risk is more acceptable in the context of a trial of a potentially effective medicine, even when the performance characteristics of the risk predictors will be validated during the course of the same trial. With successful validation of the genetic test, future drug trials can be enriched for high-risk individuals allowing for fewer test subjects, trials conducted within shorter timeframes and at lower costs.

Several studies have been launched recently to investigate the impact of genetic information on risk perception and changes in behavior (reviewed in [39]). deCODE Genetics (Reykjavik, Iceland), in collaboration with Duke University (NC, USA), initiated a study involving 1000 participants to "assess the clinical utility of a genetic test for Type 2 diabetes risk in combination with standardized risk assessment compared with standardized risk

assessment alone, and to measure whether changes in perceived risk following genetic testing for Type 2 diabetes risk are correlated with behavior change and increased concern about risk for Type 2 diabetes" [102]. A second initiative, from the Scripps Translational Science Institute (CA, USA) and Navigenics (CA, USA) together with Affymetrix® (CA, USA) and Microsoft (WA, USA), aims to assess the impact of personal genetic testing on the behavior of up to 10,000 participants. These individuals choose to receive an assessment of their genetic risk for health conditions that may be changed by lifestyle (e.g., diabetes, obesity, heart attack and some forms of cancer). The participants will be followed over a 20-year period. A potential bias of this study is that individuals are Scripps' employees who may disproportionately express favorable attitudes towards genetic testing and may differ significantly from the general population with respect to socioeconomic and educational status [103].

Prospective studies are long term, but only when such strategies are implemented will the medical community generate more confidence in the usefulness of predictive genetic diagnostics. In the meantime, we rely on data that suggest that any psychological harm resulting from genetic testing is not that serious and can be addressed by proper counseling. Each person has a right to know about his or her genetic peculiarities and the right to decide what to do with this knowledge. Gaining experience with how to deal with genetic information will provide a greater opportunity for genomic medicine to succeed in the future.

Future perspective

With time, personal genomic information will find its appropriate place in medicine. Key genetic markers for many diseases will be discovered, validated prospectively and introduced into risk assessment models. More pharmacogenetic markers will be introduced, affording personalized disease treatment or prevention plans. There will always be a big difference between how low-penetrance polymorphisms versus high-penetrance mutations are used in clinical practice. Although it appears that genetic information has limited impact on behavior, there is, and will continue to be, great interest in personal genotyping.

Acknowledgements

We are grateful to our respondents for participating in the survey and sharing their thoughts about the future of predictive genetic testing. We thank Dr Sergey V Skripin, Department of Theoretical Cybernetics of the Tomsk State University (Russia), for statistical advice and Dr Donna G Crenshaw, Deane Drug Discovery Institute, Duke University Medical Center (NC, USA), for valuable discussion and advice on manuscript preparation. We are grateful to the anonymous reviewers for their helpful comments.

Financial & competing interests disclosure

This work was supported by The Research Institute of Medical Genetics SB RAMS and The Russian Federal Agency for Education (#P-713). The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

No writing assistance was utilized in the production of this manuscript.

Executive summary

Public interest in genetic testing for common diseases

- All the published studies of public attitudes reveal a high level of interest for individual genotyping.
- A highly positive response to a question regarding genetic risk assessment for avoidable diseases was revealed in a Russian urban population.
- In the Russian public, women were demonstrated to be more supportive of personal genotyping and disease risk assessments than men.
- Younger people and those with poor health are more likely to opt for testing; educational level and marital status have no effect.

Factors that influence people's decisions to undergo genetic testing for disease predisposition

- Anxiety about health is the primary motivator for undergoing genetic testing for common health conditions.
- Wanting to know about probable future diseases, readiness to improve lifestyles and an interest in learning about personal genome characteristics are important predictors for wanting to be tested.

Possible risks & harms of predictive genetic testing

- Although there were many early presumptions about possible unfavorable outcomes of predictive genetic testing, there is evidence that psychological harms are not as serious as feared and can be diminished with appropriate pre- and post-testing counseling.
- Most of the genome-based tests currently available are not designed for use by people without disease symptoms. Testing healthy people without assessing other risk factors can cause serious harm.
- With the low predictive abilities of currently available genetic tests, proper interpretation of the data and genetic counseling are essential.
- There is a need for prospective validation of genetic panels used for risk assessments and additional efforts to measure the effects of genetic information disclosure and how this information might contribute to lifestyle changes.

Bibliography

Papers of special note have been highlighted as:
- ▪ of interest
- ▪▪ of considerable interest

1 Haga SB, Khoury MJ, Burke W: Genomic profiling to promote a healthy lifestyle: not ready for prime time. *Nat. Genet.* 34, 347–350 (2003).

2 McGuire AL, Burke W: An unwelcome side effect of direct-to-consumer personal genome testing: raiding the medical commons. *JAMA* 300, 2669–2671 (2008).

3 Grosse SD, Khoury MJ: What is the clinical utility of genetic testing? *Genet. Med.* 8, 448–450 (2006).

4 Offit K: Genomic profiles for disease risk: predictive or premature? *JAMA* 299, 1353–1355 (2008).

5 Borry P, Evers-Kiebooms G, Cornel MC, Clarke A, Dierickx K: Genetic testing in asymptomatic minors. *Eur. J. Hum. Genet.* 17, 711–719 (2009).

6 Gurwitz D, Bregman-Eschet Y: Personal genomics services: whose genomes? *Eur. J. Hum. Genet.* 17, 883–889 (2009).

7 Evans JP, Green RC: Direct to consumer genetic testing: avoiding a culture war. *Genet. Med.* 11, 568–569 (2009).

8 Ng PC, Murray SS, Levy S, Venter JC: An agenda for personalized medicine. *Nature* 461, 724–726 (2009).

▪ **Compares the results of two direct-to-consumer companies on risk assessments for 13 diseases in five individuals, and proposes several recommendations based on their findings for both direct-to-consumer companies and the scientific community on how to improve genetic diagnostics.**

9 Khoury MJ, McBride CM, Schully SD *et al.*: The scientific foundation for personal genomics: recommendations from a national Institutes of Health Centers for Disease Control and Prevention multidisciplinary workshop. *Genet. Med.* 11(8), 559–567 (2009).

10 Sanderson SC, Wardle J, Jarvis MJ, Humphries SE: Public interest in genetic testing for susceptibility to heart disease and cancer: a population-based survey in the UK. *Prevent. Med.* 39(3), 458–464 (2004).

11 Berth H, Balck F, Dinkel A: Attitudes toward genetic testing in patients at risk for HNPCC/FAP and the German population. *Genet. Test.* 6, 273–280 (2002).

12 Aro AR, Hakonen A, Hietala M *et al.*: Acceptance of genetic testing in a general population: age, education and gender differences. *Patient Educ. Couns.* 32, 41–49 (1997).

13 Henneman L, Timmermans DRM, Van Der Wal G: Public attitudes toward genetic testing: perceived benefits and objections. *Gen. Testing.* 10(2), 139–145 (2006).

14 Jallinoja P, Aro AR: Does knowledge make a difference? The association between knowledge about genes and attitudes toward gene tests. *J. Health Comm.* 5, 29–39 (2000).

15 Wilde A, Meiser B, Mitchell PB, Schofield PR: Public interest in predictive genetic testing, including direct-to-consumer testing, for susceptibility to major depression: preliminary findings. *Eur. J. Hum. Genet.* 18, 47–51 (2010).

16 Gollust SE, Hull SC, Wilfond BS: Limitations of direct-to-consumer advertising for clinical genetic testing. *JAMA* 288, 1762–1767 (2002).

17 Brunger JW, Murray GS, O'Riordan M, Matthews AL, Smith RJ, Robin NH: Parental attitudes toward genetic testing for pediatric deafness. *Am. J. Hum. Genet.* 67, 1621–1625 (2000).

18 Umans-Eckenhausen MA, Oort FJ, Ferenschild KC, Defesche JC, Kastelein JJ, de Haes JC: Parental attitude towards genetic testing for familial hypercholesterolaemia in children. *J. Med. Genet.* 39(9), E49 (2002).

19 Elwood JM: Public health aspects of breast cancer gene testing in Canada. Part 2: selection for and effects of testing. *Chronic. Dis. Can.* 20(1), 14–20 (1999).

20 Neumann PJ, Hammitt JK, Mueller C *et al.*: Public attitudes about genetic testing for Alzheimer's disease. *Health Aff. (Millwood)* 20(5), 252–264 (2001).

▪▪ **Examines the interest in a hypothetical predictive test for Alzheimer's disease in the general population.**

21 Makeeva OA, Markova VV, Puzyrev VP: Public interest and expectations concerning commercial genotyping and genetic risk assessment. *Pers. Med.* 6(3), 329–341 (2009).

▪▪ **Earlier paper published on the survey's results of the Russian general public's attitude towards different aspects of predisposition genetic testing.**

22 Stewart-Knox BJ, Bunting BP, Gilpin S *et al.*: Attitudes toward genetic testing and personalized nutrition in a representative sample of European consumers. *Br. J. Nutr.* 101, 982–989 (2008).

23 Meiser B, Kasparian NA, Mitchell PB *et al.*: Attitudes to genetic testing in families with multiple cases of bipolar disorder. *Genet. Test.* 12(2), 233–243 (2008).

24 Lerman C, Biesecker B, Benkendorf JL *et al.*: Controlled trial of pretest education approaches to enhance informed decision-making for *BRCA1* gene testing. *J. Natl. Cancer. Inst.* 89, 148–157 (1997).

25 Bernhardt C, Schwan AM, Kraus P, Epplen JT, Kunstmann E: Decreasing uptake of predictive testing for Huntington's disease in a German centre: 12 years' experience (1993–2004). *Eur. J. Hum. Genet.* 17(3), 295–300 (2009).

26 Creighton S, Almqvist EW, MacGregor D *et al.*: Predictive, pre-natal and diagnostic genetic testing for Huntington's disease: the experience in Canada from 1987 to 2000. *Clin. Genet.* 63(6), 462–475. (2003).

27 Toiviainen H, Jallinoja P, Aro AR, Hemminki E: Medical and lay attitudes towards genetic screening and testing in Finland. *Eur. J. Hum. Genet.* 11, 565–572 (2003).

28 Press NA, Yasui Y, Reynolds S, Durfy SJ, Burke W: Women's interest in genetic testing for breast cancer susceptibility may be based on unrealistic expectations. *Am. J. Med. Genet.* 99(2), 99–110 (2001).

29 McBride CM, Alford SH, Reid RJ, Larson EB, Baxevanis AD, Brody LC: Characteristics of users of online personalized genomic risk assessments: implications for physician–patient interactions. *Genet. Med.* 11(8), 582–587 (2009).

▪ **Presents results of a population-based study that prospectively evaluated effects of offering genetic testing for multiple health conditions to a large and heterogeneous population of healthy people.**

30 Heshka JT, Palleschi C, Howley H, Wilson B, Wells PS: A systematic review of perceived risks, psychological and behavioral impacts of genetic testing. *Genet. Med.* 10, 19–32 (2008).

31 Ulrich CM, Kristal AR, White E, Hunt JR, Durfy SJ, Potter JD: Genetic testing for cancer risk: a population survey on attitudes and intention. *Comm. Genet.* 1, 213–222 (1998).

32 Wilhelm K, Meiser B, Mitchell PB *et al.*: Issues concerning feedback about genetic testing and risk of depression. *Br. J. Psychiatry.* 194(5), 404–410 (2009).

33 Nelson HD, Huffman LH, Fu R, Harris EL: Genetic risk assessment and *BRCA* mutation testing for breast and ovarian cancer susceptibility: systematic evidence review for the U.S. Preventive services task force. *Ann. Intern. Med.* 143, 362–379 (2005).

34 Green RC, Roberts JS, Cupples LA *et al.*: Disclose of *APOE* genotype for risk of Alzheimer's Disease. *N. Engl. J. Med.* 361(3), 245–254 (2009).

▪▪ **Results of a prospective study that examined the effect of *APOE* genotype disclosed to the adult progeny of patients with Alzheimer's disease.**

35 Mayeux R, Saunders AM, Shea S *et al.*: Utility of the apolipoprotein E genotype in the diagnosis of Alzheimer's disease. Alzheimer's Disease Centers Consortium on Apolipoprotein E and Alzheimer's Disease. *N. Engl. J. Med.* 338(8), 506–511 (1998).

36 Post SG, Whitehouse PJ, Binstock RH *et al.*: The clinical introduction of genetic testing for Alzheimer disease. An ethical perspective. *JAMA* 277(10), 832–836 (1997).

37 Lutz MW, Crenshaw D, Saunders AM, Roses AD: Structural variants and risk for complex disease: Alzheimer's disease as a model for autosomal codominant traits. *Alzheimer's Dementia* 6, 125–113 (2010).

38 Roses AD, Lutz MW, Amrine-Madsen H *et al.*: A *TOMM40* variable-length polymorphism predicts the age of late-onset Alzheimer's disease. *Pharmacogenomics J.* 22, 1–10 (2009).

39 Caulfield T, Ries NM, Ray PN, Shuman C, Wilson B: Direct-to-consumer genetic testing: good, bad or benign? *Clin. Genet.* 77(2), 101–105 (2010).

Websites

101 23andMe & Navigenics' Open Letter to *Nature*
http://spittoon.23andme.com/2009/11/18/23andme-navigenics-open-letter-to-nature

102 Effect of Type 2 Diabetes Genetic Risk Information on Health Behaviors and Outcomes (TDE)
http://clinicaltrials.gov/show/NCT00849563

103 Navigenics (press release): Landmark research study is launched to assess impact of personal genetic testing. CA, USA, 9 October (2008)
http://www.navigenics.com/visitor/about_us/press/releases/scripps_study_release_100908/

104 US public opinion on uses of genetic information and genetic discrimination
www.dnapolicy.org/resources/GINAPublic_Opinion_Genetic_Information_Discrimination.pdf

105 Human Genetics Commission: Genes direct. Ensuring the effective oversight of genetic tests supplied directly to the public (2003)
www.hgc.gov.uk/UploadDocs/DocPub/Document/genesdirect_full.pdf

106 Freedman D, Furness P, Green A *et al.*: *Making Sense of Testing: A Guide to Why Scans and Health Tests For Well People Aren't Always A Good Idea*. Sense About Science, London, UK (2008)
www.senseaboutscience.org.uk/pdf/makingsenseoftesting.pdf

▪▪ **Presents an expert overview of arguments and reasons why most of tests are not designed to be used by healthy people.**