# A practice model for personalized healthcare with a public health genomics perspective

Epidemiological and demographic transition has brought populations to an extended life expectancy in the 21st Century. The diseases of this century are complex, which stem mainly from the complex interactions of the human genome with lifestyle and environmental factors. These diseases are common, chronic and costly. Currently, the best-known prevention for complex diseases is adopting a healthy lifestyle. However, this is not achieved in many places in the world. Effective intervention models, including lifestyle changes for the prevention of these diseases, is urgently needed. In this report, we introduce a preventive healthcare model based on personalized healthcare. It is based on the application of public health genomics tools and concepts on an individual level, in order to stratify individuals according to risk groups, prevent diseases and detect them early.

**KEYWORDS: chronic complex diseases ■ genetic predispositions ■ nutrigenetics ■ personalized healthcare ■ public health genomics**

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Life expectancy has been steadily increasing in almost all regions of the world since the beginning of the 20th Century. This happened as a result of epidemiologic and demographic transition in the world [1]. In the beginning of the 20th Century, life expectancy was below 50 years in western countries, whereas today it is above 75 years. Populations are rapidly aging.

The diseases of the 21st Century are chronic and complex, which stem mainly from the complex interaction of the human genome with lifestyle factors. Cardiovascular and cerebrovascular diseases, cancers, diabetes, obesity, osteoporosis, neurodegenerative diseases and psychiatric diseases are among major chronic and complex diseases, which account for approximately 84% of deaths and 76% of the burden of disease in high- and upper-middle-income countries [101]. The prevalence of chronic diseases increases significantly with age. Thus, the 21st Century brings us to an aged population living with chronic conditions, creating a huge burden on healthcare systems and society. Complex diseases are not only the problem of high-income/industrialized countries, but also low-income countries in the process of industrialization.

One of the biggest challenges of the health and social systems of the 21st Century is to add productivity and life quality to prolonged life years, while keeping the healthcare costs under control by reducing the burden of complex diseases. The solution lies in preventive interventions that start in earlier ages, much earlier than the onset of the complex diseases. As the most important preventive measure, individuals must follow an appropriate and personal lifestyle plan. Giving general information and recommendations on health issues to the public has limited effectiveness to change the lifestyle of individuals. Therefore, an effective intervention model including lifestyle changes for prevention of these diseases is urgently needed.

## Complex diseases, genetics & personalized healthcare

### ■ Complex diseases & genetics

Complex diseases are caused by the interaction of genetics with the lifestyle of an individual. In order to understand the genetic basis of diseases, we can visualize the diseases in a threshold model, as shown in Figure 1. Here, diseases are grouped into three major areas, according to the disease-causing factors.

The first group of diseases are caused by alterations in the genetic structure of human beings. Down's syndrome and cystic fibrosis are disorders caused by deleterious changes in the genes associated with the diseases. They constitute a small fraction of the burden of disease. External factors play little or no role in most of these diseases. With today's conditions, there is limited space for measures to prevent the disease occurrence in individuals carrying a genetic abnormality (see first column in Figure 1).

The second group of diseases are caused directly by external factors such as infectious diseases, injuries, poisonings and so on (see second column in Figure 1). Genetics has a very limited

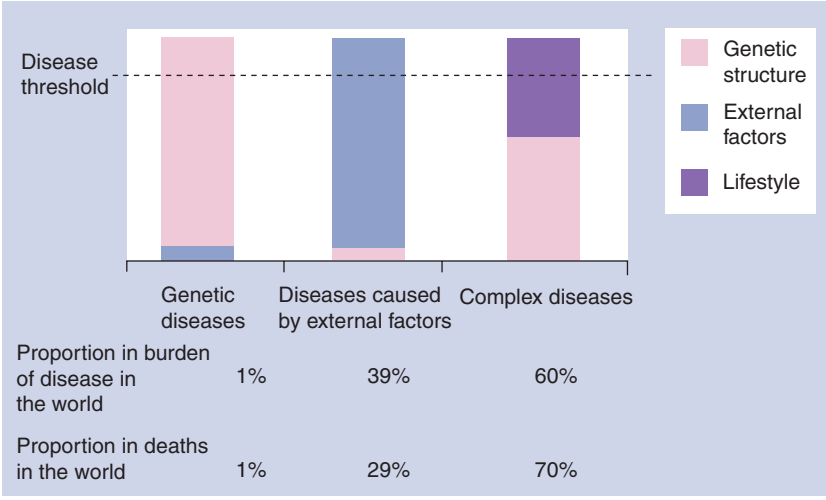


**Figure 1. Diseases, genes, environment and lifestyle interaction from a disease threshold perspective.**

role in these conditions. This group, especially infectious diseases within it, was the major burden of disease before the industrial revolution. The burden of disease caused by this group has reduced relatively, parallel to the developments in science and technology such as sanitation, antibiotics and vaccines.

The third group consists of disorders where common variations in genetic structure (polymorphisms) create a predisposition to the disease, but cannot cause the disease without other factors, mainly unfavorable lifestyle factors of individuals (see third column in Figure 1). Because of this complex nature of gene–lifestyle interaction, they are called complex diseases. Main examples include cardiovascular and cerebrovascular diseases, diabetes, osteoporosis, cancers, neurological conditions and psychiatric disorders, which are mostly late-onset chronic diseases. They arise from an individual's lifestyle and environmental factors imposed on their genetic predisposition. They consist of a large proportion of burden of disease all over the world. The burden of chronic complex diseases will continue to expand steadily as a result of demographic and epidemiological transition in the next 20 years [101].

## Opportunities for the use of genetics in complex diseases

Since the successful completion of the Human Genome Project, we have an exponentially increasing understanding of genetic factors and complex diseases. The identification of new genes and polymorphisms that have influence in diseases is helping to understand the underlying biology of the diseases, and leading to new therapeutic approaches, as well as understanding of how genetic variations are of influence in predisposition of different individuals to different diseases. The knowledge regarding associations of polymorphisms with complex diseases is constantly growing.

One of the success factors of nutritional interventions is prediction of the response of the individual to specific interventions. At this point, nutrigenetics is expected to play a major role. Nutrigenetics, which studies an individual's specific response to diet owing to genetic variants (polymorphisms) [2], is positioned as the emerging face of nutrition that, when considered with more classical approaches, will provide the necessary stepping stones to achieve the ambitious goal of optimizing an individual's health. Similarly, pharmacogenetics will allow us to tailor the pharmacological interventions according to the specific needs of individuals, and minimize side effects while maximizing efficacy.

The strong interaction of biological and genetic factors with lifestyle factors in the development of chronic and complex diseases has brought us to a new understanding of 'genetics', where genetics is not only related to the study of rare hereditary disorders, as understood in 'conventional' medical genetics. In the late 1990s and early 2000s, it was foreseen that genetics/genomics would revolutionize medicine [3–5], and that genetics would become a tool widely used for prediction, diagnosis and the optimization of treatment in most common diseases within the current decade [3,4].

New issues and problems arise related to various aspects of this new potential practice; such as practice models of complex genetics, nutrigenetics and pharmacogenetics; clinical utility and validity of genetic tests; and ethical, legal and social aspects. They fall under the area of public health genomics, which is defined as a multidisciplinary field concerned with the effective and responsible translation of genome-based knowledge and technologies to improve population health [102]. Public health genomics uses population-based data on genetic variation and gene–environment interactions to develop evidence-based tools for improving health and preventing disease [103].

One of the most promising implication areas of genomics lies in preventive healthcare, especially for complex diseases. Applications of personalized medicine combined with the advent of health information technology in clinical practice will bring a new kind of medical care: personalized healthcare [104]. It is healthcare that works better for each patient, based partly on

scientific information that is new, and partly on technology to make complex information useful [104].

## Facts & challenges for the use of genetics in complex diseases

As we are approaching the end of the decade, science has made important progress in the discovery of genes and polymorphisms. However, their integration into medical practice has been limited. Current examples of the usage of common polymorphisms in clinical practice are polymorphisms in *F5* (Factor V), *F2* (Factor II) and *MTHFR* for thrombophilia and perinatology; *APOE* for cardiovascular risks and Alzheimer's disease risk; and *CYP2C9*, *CYP2C19* and *CYP2D6* for pharmacogenetics. Limited use of polymorphisms in medical practice has been the result of the fact that evidence demonstrating the effectiveness in clinical use is not fully established yet. On the other hand, the current knowledge about the above-mentioned areas already has the potential to be used for the benefit of the individual and society.

There are limitations and room for improvement for the current scientific information. Although the knowledge about associations of polymorphisms with complex diseases is constantly growing, evidence is not fully established. Current linkage analysis and genome-wide association studies are focused merely on the genotype–disease relationship. Genotype information can be investigated together with other contributing factors for assessment of disease risks (lifestyle including smoking, nutrition, and exercise; personal health history; family history; environmental exposures, and so on). On the other hand, current studies investigating the interactions between genotype and lifestyle factors are bringing limited evidence owing to small sample sizes. The limited number of prospective studies demonstrates the benefit of selected nutrition or nutritional supplement use based on selected genetic structures [6]. This type of prospective intervention study is needed for various other claims regarding nutrient–genotype interactions.

Limited information suggests that personal risk assessments and personalized recommendations can be a more effective means compared with classical approaches to change the lifestyle of the individuals [7]. In addition, the current level of technology allows us to make personalized risk assessments and develop personalized recommendations based on health information of individuals, including genetic information. There are several initiatives to benefit from genetic data to make personalized risk assessments and recommendations [105–108]. However, the effectiveness of such applications has not been thoroughly evaluated (i.e., controlled prospective studies).

## Approach of GENAR Institute

As the GENAR Institute for Public Health and Genomics Research (Ankara, Turkey), we have been working on the development of a practice model called Gentest®, which is an endeavor to face the above-mentioned challenges as an integrative preventive model that utilizes an individual's health information, lifestyle factors, biomarkers and genotype in order to prevent and detect chronic and complex diseases early in a targeted way [8] (for information on GENAR Institute, see Box 1).

The mission of this practice model is changing the behavior and managing the health of individuals according to their health priorities.

The conceptual framework of Gentest is presented in Figure 2. Its components are described in the implementation stages below.

Gentest is designed to be implemented in primary-care settings where the health professional(s) (physicians and/or dieticians) can focus on preventive healthcare interventions. For the piloting phase of the model, it is mainly practiced in the Gentest Implementation Center, which is run by GENAR. In addition, health professionals are authorized to be practitioners of Gentest after participating in training of the Turkish Society of Public Health Genomics and Nutrigenetics and the GENAR Institute.

The diseases/health areas that are undertaken in Gentest are selected based on their prevalence, the burden they create and the ability to recommend lifestyle and medical interventions

**Box 1. GENAR Institute for Public Health and Genomics Research.**

The GENAR Institute for Public Health and Genomics Research was established in 2004, in Hacettepe University Science Park, Ankara, Turkey. It is the third public health genomics center in Europe and a cooperating institute of Public Health Genomics European Network (PHGEN) [110]. The GENAR Institute aims to transform scientific developments in the area of biotechnology, especially those in genetics and genomics, into products and services that improve human health, quality of life and performance, and extend lifespan. The GENAR Institute has a broad range of working area, mainly on chronic complex diseases. The R&D activities focus on understanding the underlying genetic and genomic basis of these conditions and developing products based on targeted prevention, early detection and treatment strategies.

The GENAR Institute is comprised of three centers: GENAR Biotechnology and Molecular Genetics Research and Diagnostic Laboratories, which is a high-throughput molecular genetic analysis laboratory; GENAR Center for Nutrigenetics and Lifestyle Research, which focuses on quantifying the nutrition and other lifestyle factors of individuals and developing models for personalized nutrition and lifestyle advice for optimization of individual needs; and the GENAR Center for Personalized Medicine and Pharmacogenetics, which aims to catalyze transfer of developments in genetics to the health of individuals with a public health vision. There has also been an implementation center in Istanbul, Turkey, to pilot the developed models.

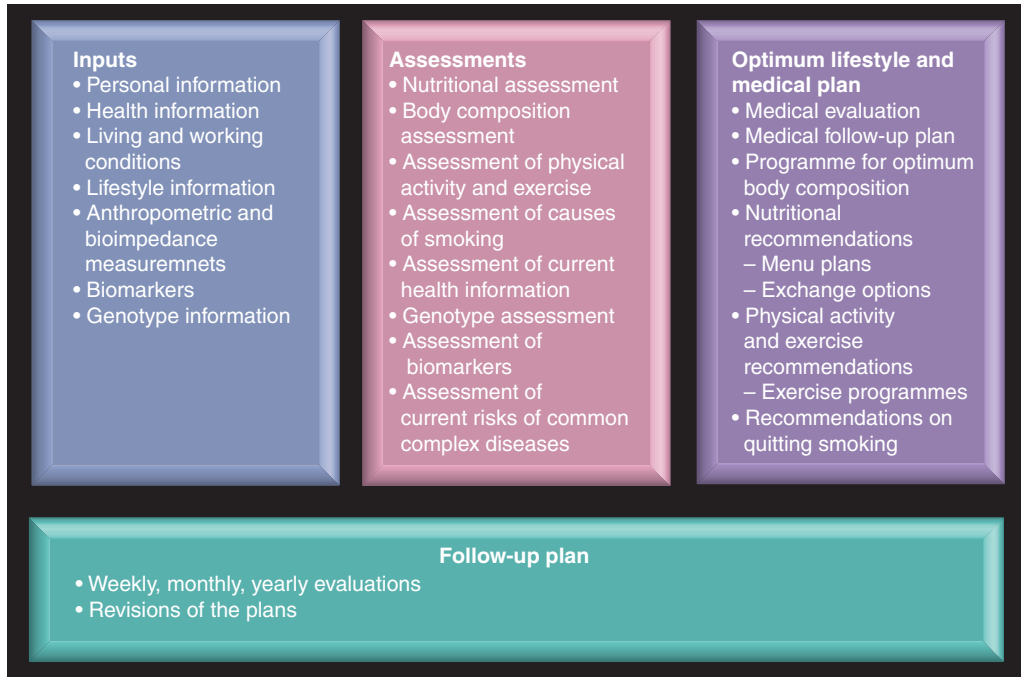


**Figure 2. Conceptual framework for the Gentest practice model.**

to reduce the risks or delay the onset of these diseases. Currently, the following diseases and health areas are undertaken in Gentest:

- Cardiovascular and cerebrovascular diseases;
- Insulin resistance, Type 2 diabetes and obesity;
- Inflammation;
- Osteoporosis;
- Antioxidation and detoxification mechanisms;
- Cancers in general, and the five most prevalent cancers in particular, which are lung, breast, prostate, colon and stomach.

## Implementation stages of the practice model

### Data & information collection stage

An individual who applies to the Gentest Implementation Center is first explained what Gentest is, and what it is not (see Table 1). The most suitable Gentest package for that individual's personal characteristics and requirements is chosen with the help of the physician.

Special attention is paid to create proper consumer expectations, as defined in Table 1. For this purpose, a sample Gentest, which is an anonym report of a real case, is presented to the individual. After oral and written acknowledgments explaining the issues summarized in Table 1, the individual signs the consent form for DNA analysis. An appointment is given to come with overnight fasting.

When the person comes to the appointment, blood and urine samples are taken. Anthropometric measurements are made using scales and a tape measure, and bioelectrical impedance is used for body composition analysis. Blood pressure and pulse is measured. The individual fills in a detailed questionnaire collecting the necessary inputs listed in Box 2 with the assistance of a health professional. Gentest Food Portion Atlas (Figure 3), which is developed by GENAR, is used during collection of food consumption data. It takes approximately 2 h for measurements and filling in the information form.

Blood and urine biomarker analysis are carried out by an external biochemical laboratory and the results are forwarded to the GENAR Institute. One tube of blood sample is transported to GENAR Laboratories for genetic analysis.

### Assessments

The questionnaire is analyzed by the GENAR Center for Nutrigenetics and Lifestyle Research, to quantify the nutrient intake, physical activity status and causes of smoking. The current consumption status of macro- and micronutrients are assessed with the analysis of both food consumption records and food frequency questionnaires.

For each macro- and micro-nutrient, a minimum and maximum level of intake recommendation is determined. These nutrients include: macronutrients such as protein, carbohydrate and fat, including different saturated/unsaturated fats

**Table 1. What is Gentest and what is not?**

| What is Gentest? | What is not Gentest? |
|---|---|
| Gentest is developed to assist health professionals and the individual in their efforts to prevent diseases and promote health | – |
| Gentest recommendations are subject to the evaluation of and can be changed by the health professional | – |
| Gentest can only be implemented through authorized health professionals (physician and/or dieticians, according to the content of the packages) | Gentest is not a direct-to-consumer service |
| Gentest provides information on disease predispositions and risks | Gentest does not diagnose diseases or give treatment advice. Gentest does not provide deterministic information if a person will develop a disease or not |
| The main purposes of the risk calculations are to provide the lifestyle and medical follow-up interventions in a targeted way and to create individual risk perception | – |
| Gentest gives personal recommendations to decrease one's health risks and lead a healthier life within their own genetic make-up | Being predisposed to a disease does not mean that the person will definitely develop it |
| Risk calculations are based on population studies and refer to the risk of subgroups of individuals carrying the characteristics of the individual subject to the test. The characteristics used for the calculations are: age, gender, health information, biomarkers, lifestyle factors and genetic make-up | Carrying the risk of the disease does not mean that the person will definitely develop it |
| Based on the current scientific knowledge, following the medical follow-up and lifestyle recommendations given in the Gentest report reduces one's disease risks | Following the medical follow up and lifestyle recommendations given in the Gentest report does not completely eliminate one's risks |

and omega 6/omega 3 fatty acids; vitamins; minerals; and key functional foods. Recommended levels are based on age, gender, current diseases, genetic information and lifestyle information of the individuals. Recommendation algorithms are based on international and national guidelines on macro- and micro-nutrients and literature on nutrition and nutrigenetics research. The recommendations are presented both in tables and figures (for an example of figures, see Figure 4).

Assessment on body composition is made using anthropometric measurements and bioimpedance analysis (Figure 5).

Current exercise status related to eight different areas of physical fitness is assessed. These areas are cardiorespiratory fitness, muscle strength, bone strength, muscle endurance, flexibility, balance, insulin sensitivity and body composition. Currently, this assessment is based on the type, intensity, duration and frequency of the exercises carried out by the individual. More objective methods to assess the physical fitness levels of the individual are under development. The recommended level of exercise for each physical fitness area is determined according to disease risks, genetic predispositions and personal preferences (Figure 6).

If the individual is smoking, causes of smoking are also assessed using questionnaires. The types of smoking assessed are nicotine craving/physiological addiction, stimulation, relaxation/pleasure, crutch/tension reduction, habit and handling (hand contact with the cigarette).

In parallel to assessment of the lifestyle information, genetic analysis is carried out by GENAR Biotechnology and Molecular Genetics Research

**Box 2. Inputs of Gentest.**

- Personal information
  - Age
  - Gender
- Health information
  - Personal history (current and past diseases and medications)
  - Family history
- Living and working conditions
  - Occupation
  - Past and present occupational and environmental exposures
- Lifestyle information
  - Physical activity and exercise
  - Smoking and drinking habits
  - Supplement consumption
  - Nutritional habits
  - Food consumption (24 h recall and food frequency)
- Anthropometric and bioimpedance measurements
  - Height, body weight and composition
  - Waist circumference
- Biomarkers
- Genotype information

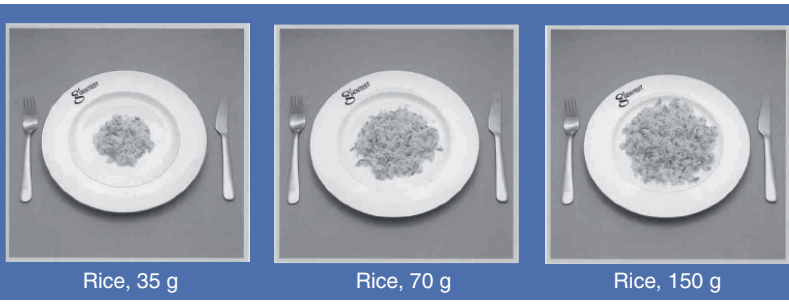


**Figure 3. An excerpt from the 'Food Portion Atlas'.**

and Diagnostic Laboratories. Genetic analysis covers common polymorphisms related to common complex diseases and conditions listed above (see Approach of GENAR Institute section). For each health area, the results are presented in a table that presents information on the gene, function/role in health-related area, polymorphism and the genotype result of the individual, as well as what the result indicates for that disease/health area (for a sample page, see Figure 7). The number of polymorphisms studied varies from 35 to 65 in the different packages.

Polymorphisms in the health area of interest are selected qualitatively based on considering a number of aspects. The studies that show a positive association and no association are evaluated in their design, statistical power, presented odds ratios and p-values, as well as the credibility of the published journal. Frequency of the polymorphism in white Caucasians are also taken into account. Studies on gene–lifestyle interactions are also evaluated with this perspective in mind.

Biochemical markers such as blood lipids, fasting plasma glucose, liver and kidney function tests, homocysteine, high-sensitivity C-reactive protein and fibrinogen are analyzed by external clinical laboratories. The biomarkers are selected and assessment methods are developed in light of the current medical guidelines and literature.

The results of lifestyle assessment, genetic analysis and biomarker tests are gathered in the GENAR Center for Personalized Medicine and Pharmacogenetics, in order to produce the report of the individuals.

In the GENAR Center for Personalized Medicine and Pharmacogenetics, risk assessments for the most common chronic complex diseases are made. These include myocardial infarction, stroke, Type 2 diabetes, osteoporosis and the five most common cancers (lung, breast, prostate, colon and stomach). Risk assessment algorithms are based on risk factors conveyed by various epidemiological studies and risk assessment models. The genetic analysis results are also used as a factor in risk assessment, but with very small effect sizes given the limited demonstrated effect of discovered polymorphisms on overall risks of diseases. The inputs of the risk assessment algorithms are listed in Box 2.

Risks are presented for two cases: the estimated risk using the current data and the estimated risk for the case that the recommended optimum lifestyle and medical follow-up plan is followed (for examples of risk graphics, see Figures 8, 9 & 10)

Risk graphics (both the current and estimated reduced risk with the optimum lifestyle and medical follow-up plan) are presented in the report for two main purposes. The first one is to provide the lifestyle and medical follow-up interventions in a targeted way. The second one

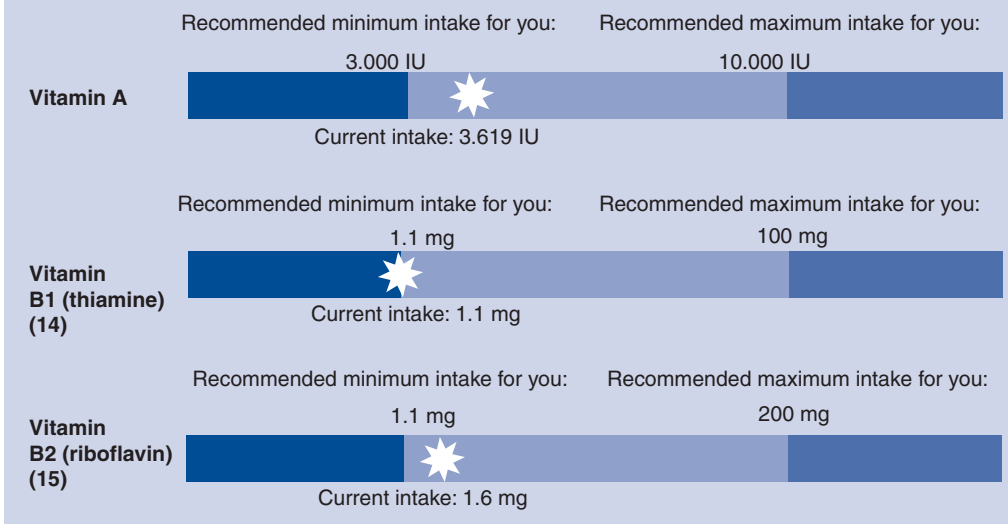


**Figure 4. An excerpt from the 'Assessment of Nutrition and Nutritional Supplements' section of a Gentest report.**

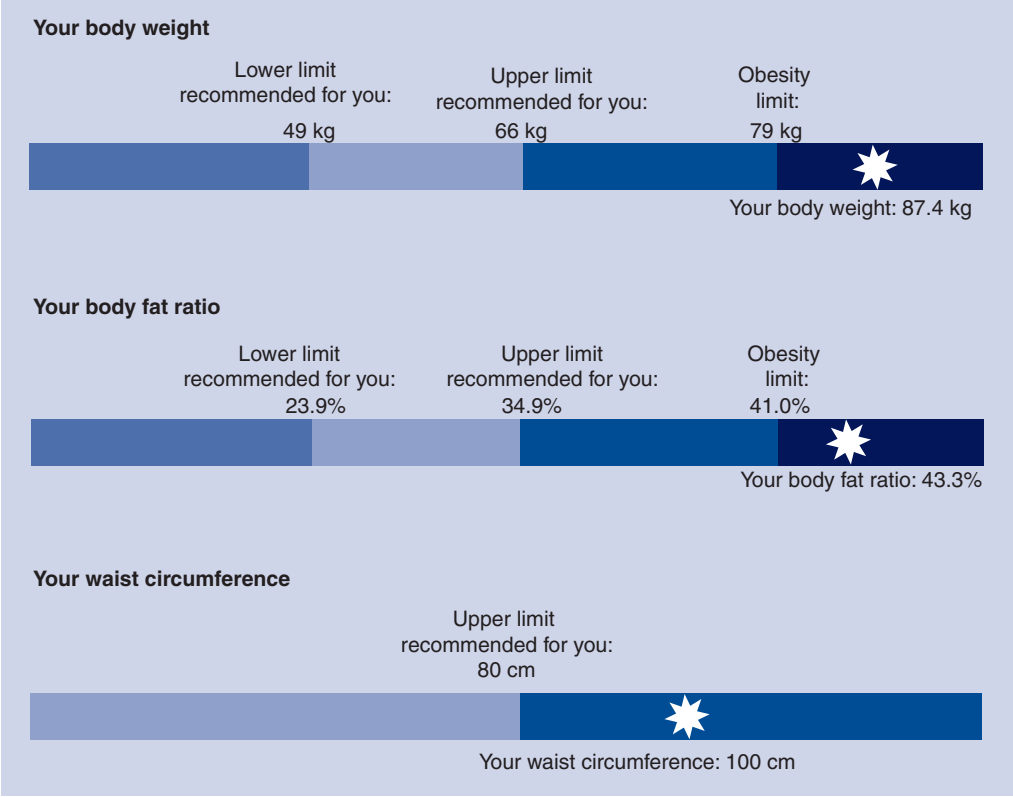


**Figure 5. An excerpt from the 'Assessment of Body Composition' section of a Gentest report.**

is to promote lifestyle changes through creating personal vulnerability perception and individual risk perception [109].

The report of an individual includes the results of the above-mentioned assessments and an 'Optimum Lifestyle Plan' developed for the individual. It includes a plan for reaching and/or maintaining optimum body composition, personal nutrition plans and food exchange lists, supplement plans and exercise plans. Smoking cessation recommendations are personalized according to the causes of smoking. Recommendations are given for medical follow-up with personalized screening plans. For all medical follow-up recommendations, it is highlighted that they are subject to evaluation of the physician and can be changed if necessary. If any medical problem that needs further investigation or curative interventions is detected, it is presented in the 'physician note', which is provided for the physician separately.

When developing methodologies for all components of Gentest, the most important decision criterion is this: for all the information and recommendations we give, there has to be good probability of benefit with no possibility of harm. This is ensured by always complying with the nutritional and medical guidelines. For example, recommendations on the upper and lower limits of the intake of a nutrient are always within the upper and lower limits that are recommended in the nutrition guidelines. Properties that can be used to further personalize the recommendations, but not referred in the guidelines yet, such as genetic information, are used to narrow down the general recommendation range.

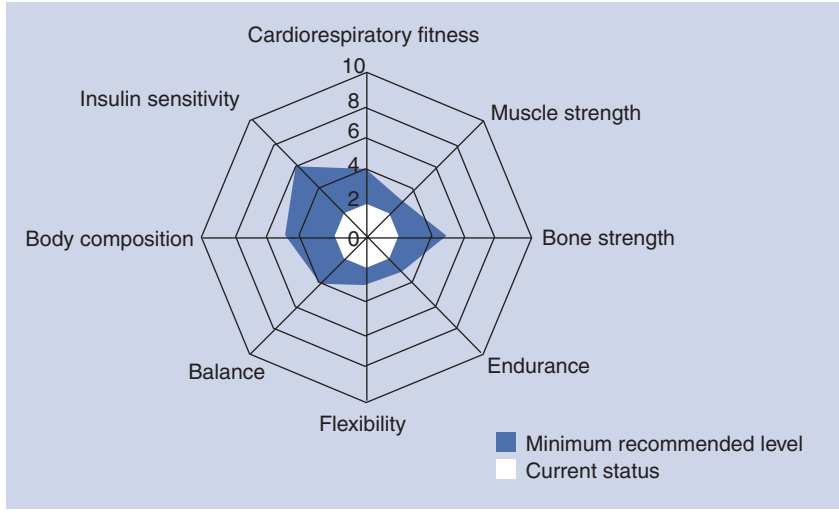


**Figure 6. An excerpt from the 'Assessment of Physical Activity and Exercise Status' section of a Gentest report.**

**1. CARDIOVASCULAR AND CEREBROVASCULAR HEALTH**

⚠ sign is used in case that genotype indicates predisposition to that condition, whereas ▲ sign is used in case of a favorable condition and <-> in case of a neutral situation. If not applicable, ∅ is used. If the predisposition to the condition decreases under some certain life style modifications or this genotype specifically responds well to a certain factor, √ sign in used under " Response to lifestyle modif." column.

| Gene | Full Name | Function / Role in Related Health Area | Analyzed Polymorphism | Genotype | Allele Structure | Atherosclerosis and Atherothrombosis | | Hypertension | | Venous Thrombosis | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Predisposition | Response to lifestyle modif. | Predisposition | Response to lifestyle modif. | Predisposition | Response to lifestyle modif. |
| APOA1 | Apolipoprotein A-I | HDL Structure; Cholesterol Metabolism | G(75)A | Homozygous | AA | ⚠⚠ | √ | ∅ | | ∅ | |
| APOC3 | Apolipoprotein C3 | HDL,LDL,VDLD Structure; Triglyceride and Cholesterol Metabolism | C3175G | No variation | CC | ▲ | | ∅ | | ∅ | |
| LPL | Lipoprotein Lipase | Lipid Metabolism | C1595G | No variation | CC | ⚠⚠ | √ | ∅ | | ∅ | |
| LIPC | Hepatic Lipase | HDL Metabolism | C(514)T | Heterozygous | C/T | ∅ | √ | ∅ | | ∅ | |
| CETP | Cholesterol Ester Transfer Protein | HDL - LDL Cholesterol Balance | G279A | Heterozygous | G/A | ⚠ | √ | ∅ | | ∅ | |
| PON1 | Paraoxanase1 | Lipid Oxidation Mechanism | Gln192Arg | No variation | Gln/Gln | ▲ | | ∅ | | ∅ | |
| MMP3 | Matrix Metalloproteinase 3 | Matrix Deposition; Atherosclerotic Mechanism | 5A/6A | No variation | 5A/5A | ▲ | √ | ∅ | | ∅ | |
| IL-6 | Interleukin-6 | Inflammatory Response | G(-174)C | Heterozygous | G/C | ⚠⚠ | √ | ∅ | | ∅ | |
| TNF-α | Tumor Necrosis Factor Alpha | Inflammatory Response | G(-308)A | No variation | GG | ▲ | | ∅ | | ∅ | |

**Figure 7. An excerpt from the 'DNA Analysis Results and Genotype Assessment Table' section of a Gentest report.**

## Counseling & follow up

Gentest reports are ready approximately 4–8 weeks after sample taking and filling out the questionnaire. The report is sent out to the physician who explains the report results to the individual during an hour long appointment. The nutrition programme is explained by a dietician trained in nutrigenetics.

If the individual would like to have assistance in making the lifestyle changes, the follow-up programme is started. This option is usually chosen by the overweight or obese individuals who are recommended to reach their optimum body composition.

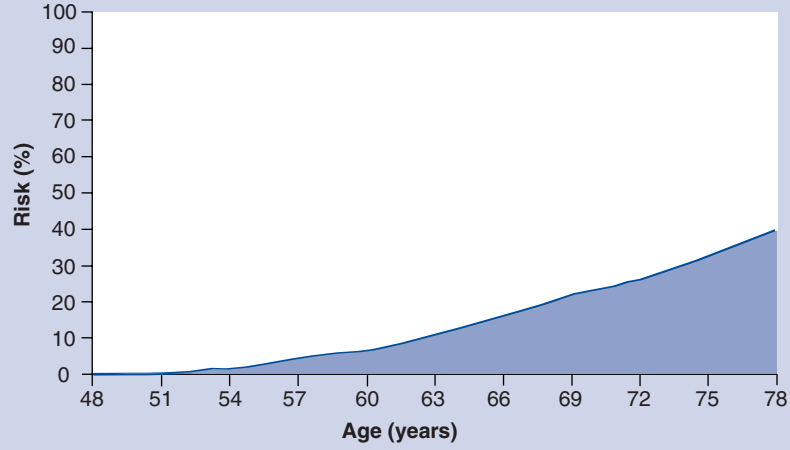


**Figure 8. An excerpt from the 'Disease Risks' section of a Gentest report: 'Heart Attack Risk with Current Lifestyle in the Following 30 Years'.**

## Experiences of GENAR

The practice model has been in service for piloting purposes for approximately 2 years in Turkey. Approximately 500 individuals have used this pilot service. The results of this pilot implementation phase are being assessed and will be published in another manuscript. A noteworthy observation is that Gentest might have a better outcome for behavior change than providing general information on healthy behaviors. In particular, initiation of exercise, smoking cessation and weight loss has been observed. This observation surely needs to be confirmed with publication of related data.

We think that Gentest may have an important effect in creating awareness by informing individuals about their current lifestyle and genetic predispositions. Furthermore, it causes an attitude change by creating a vulnerability perception. Finally, it is observed that behavior change is achieved with the follow-up programme and the trainings (Figure 11).

## Critics to the approach of the GENAR Institute

Our practice model has been presented to the scientific community at a number of occasions. These are the 1st Congress of the International Society of Nutrigenetics/Nutrigenomics (Athens, Greece, 13 November, 2007) [8], 16th European Conference on Public Health, European Public Health Association (Lisbon, Portugal, 7 November,

2008), Conference on Public Health Genomics in Europe, Public Health Genomics European Network (Istanbul, Turkey, 26 November, 2008). The practice model being comprehensive (containing several factors such as personal, medical and lifestyle information, and genetic information), multidisciplinary, prevention-orientated and implemented through health professionals have been the appraised characteristics.

On the other hand, the main critic to this practice model has been that its effectiveness has not been demonstrated yet. Since 2004, GENAR has developed the model, piloted its components and the whole model, and further developed it with feedback. This gave GENAR the chance to see if such a model is applicable in a preventive healthcare setting, and if there is a potential benefit for the consumers. Currently, we are working on the design and implementation of research for the evaluation of the effectiveness of the proposed practice model. The effectiveness will be assessed from outcome perspective (prevention of diseases and disease complications), bioprocesses perspective (lipid profile, inflammation, glycemic control and so on), lifestyle changes and applicability. Collaboration with cohorts are also planned to further develop the algorithms.

## Conclusion

Public health genomics and personalized healthcare will play major role in combating the chronic complex disease burden of the aging populations of the 21st Century. In parallel to exponentially increasing knowledge gained through research, healthcare systems need to foresee these upcoming developments and prepare for the transition. The approach of GENAR is an example of the translation of genome-based knowledge into preventive healthcare. The definition of public health genomics suggests that this translation should be effective and responsible [102]. By assuring that the information and the recommendations has good probability of benefit but has no possibility of harm, the Gentest practice model can be considered as a responsible one. However, the effectiveness has not yet been demonstrated.

## Future perspective

As the populations continue to age, the burden created by complex diseases will increase. The future healthcare systems will not be able to cope with the societal and economic burden of complex diseases. An effective intervention model including lifestyle changes for prevention of these diseases is urgently needed. Like we did a century ago with the vaccines against infectious diseases, the world needs a cost-effective health intervention to prevent complex diseases, as well as decrease the disability and increase the life quality of aging populations.

In order to achieve this goal, the medicine of the future needs to target the individual, rather than general public or population subgroups. Thus, healthcare practice models need to be individualized, assessing different characteristics

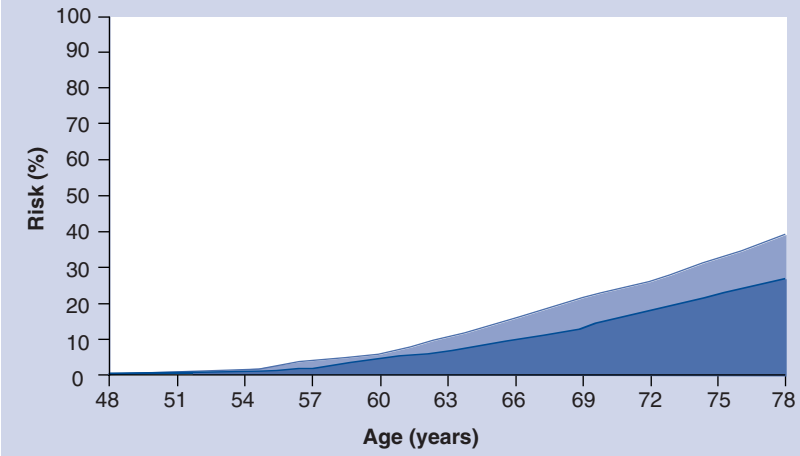


**Figure 9. An excerpt from the 'Disease Risks' section of a Gentest report: 'Reduction of Heart Attack Risk in the Following 30 Years After Implementation of Optimum Lifestyle and Medical Follow-up Plan'.**

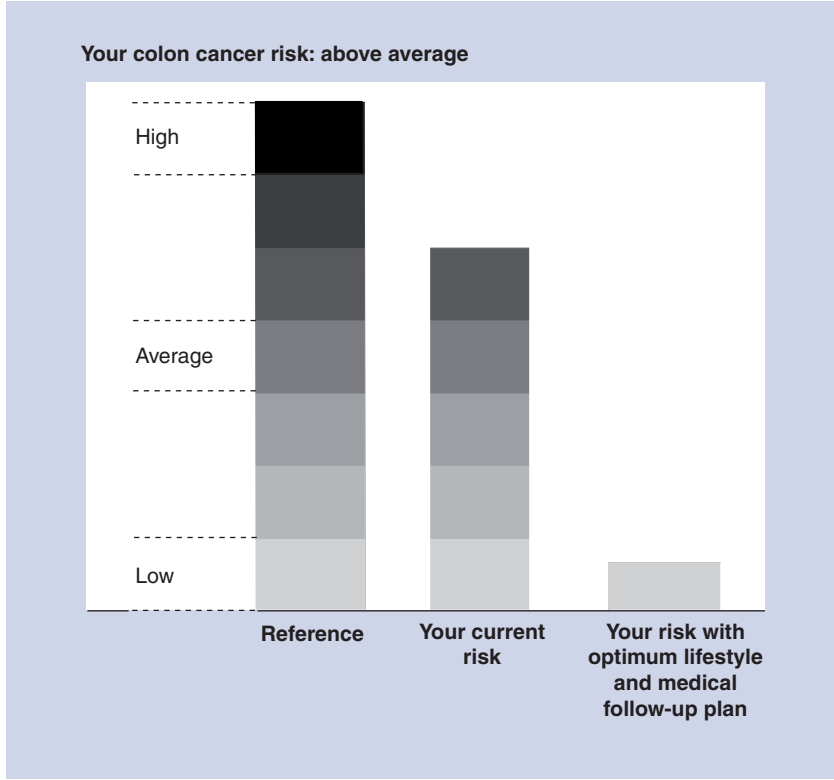


**Figure 10. An excerpt from 'Disease Risks' section of a Gentest report: 'Colon Cancer Risk'.**

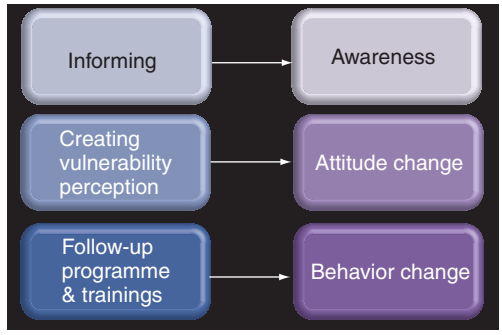


**Figure 11. Model of attitude and behavior change with Gentest.**

of the individuals, such as personal health data, lifestyle information and genetic information, to provide individualized interventions and recommendations. This vision is defined as 'personalized healthcare'.

Personalized healthcare holds great potential to combat the burden of complex diseases. In 5–10 years time, personalized healthcare interventions are expected to be widely utilized in primary care settings for primary and secondary prevention of complex diseases and their complications.

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## Financial & competing interests disclosure

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## Executive summary

***The need for effective intervention models to combat complex diseases***

- Complex diseases, which stem mainly from the complex interaction of the human genome with lifestyle and environmental factors, cause the main burden of disease in the 21st Century. Currently, the best-known prevention for complex diseases is adopting a healthy lifestyle. However, this is not achieved in many places of the world. Effective intervention models including lifestyle changes for prevention of these diseases is urgently needed.

***Facts & challenges for the use of genetics in complex diseases***

- In the late 1990s and early 2000s, it was foreseen that genetics/genomics would revolutionize medicine, and genetics would become a tool widely used for prediction, diagnosis and to optimize treatment in most common diseases within the current decade. As we are approaching the end of the decade, science has made important progress to discover genes and polymorphisms. However, their integration to medical practice has been limited, owing to the fact that evidence demonstrating the effectiveness of the genomic markers in clinical use is not fully established yet. On the other hand, the current knowledge about the above-mentioned areas already has the potential to be used for the benefit of the individual and society.

***Approach of the GENAR Institute***

- The GENAR Institute for Public Health and Genomics Research has developed a practice model called Gentest® as an integrative preventive model which utilizes individual's health information, lifestyle factors, biomarkers and genotype in order to prevent and early detect chronic and complex diseases in a targeted way. Based on the results of the aforementioned components, an optimum lifestyle plan is developed, including personal menu plans and exchange lists, exercise plans, smoking cessation recommendations based on the individual causes of smoking, and a medical follow-up plan.
- The mission of this practice model is changing the behavior and managing the health of individuals according to their health priorities. It is thought that the model creates awareness by informing individuals about their current lifestyle and genetic predispositions. Furthermore, it causes an attitude change by creating a vulnerability perception. Finally, it is observed that behavior change is achieved with the follow-up program and the trainings.

***Critics to the approach of GENAR Institute***

- The practice model being comprehensive (containing several factors of the individual), multidisciplinary, prevention orientated and implemented through health professionals have been the appraised characteristics. On the other hand, a critical point is raised, which is that the effectiveness of the intervention is not yet demonstrated.
- The efforts of GENAR so far has been on the development of the model and piloting its components and the whole model. The crucial future step is to conduct a research for evaluation of the effectiveness of the proposed practice model.

***Conclusion***

- Personalized healthcare holds a great potential to combat the burden of complex diseases, provided that the safety is ensured and the effectiveness of the utilized tests and practice models are demonstrated scientifically.

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

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▪▪ **This is the first document defining the framework of public health genomics. The Public Health Genomics Foundation (UK) website is a valuable resource for scientists and health professionals who would like to learn the concept of public health genomics, policy issues related to public health genomics, evaluation of complex biomarkers and genetic tests (www.phgfoundation.org).**

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▪▪ **CDC Office of Public Health Genomics website is a valuable resource for scientists, health professionals and the general public who would like to learn the concept of public health genomics, its scientific basis, its implementation areas and reach educational resources (www.cdc.gov/genomics/).**

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▪▪ **Important document defining the concept and vision of personalized healthcare, outlining its opportunities, the pathways to reach this vision and resources already in play within US Department of Health and Human Services. The Personalized Health Care Initiative website is a good resource to follow the reports and activities of US Department of Health and Human Services on this area (www.hhs.gov/myhealthcare/).**

105 23andMe www.23andme.com

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▪ **It is of note that there are different initiatives on the usage of genomic information in the optimization of nutrition in clinical settings. One of them is the EuroGENE project funded under the E-Ten Scheme of the EU. The overall aim of EuroGENE is to validate in the European market the existing service, as well as to enhance both its security and user friendliness. The project has three pilot sites in Italy, Germany and Greece. Results of the project are expected to be disseminated soon.**

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▪ **This short article can be a useful review to get acquainted with concepts in behavior change in health, in particular, risk perception.**

110 Public Health Genomics European Network (PHGEN) www.phgen.eu

▪ **Public Health Genomics European Network (PHGEN) is an important network working for the development of Public Health Genomics in Europe. PHGEN is coordinated from the European Centre of Public Health Genomics (ECPHG) at Maastricht University in the Netherlands. PHGEN is funded by the General Directorate for Health and Consumer Protection (DG SANCO) under the Health Programme. The current phase of PHGEN focuses on preparation of the 'European Best Practice Guidelines for Quality Assurance, Provision and Use of Genome-based Information and Technologies'.**