

Genetic Testing and Personalized Nutrition System for Men's Health Care

Jitao Yang(✉)

School of Information Science, Beijing Language and Culture University, Beijing 100083, China
yangjitao@blcu.edu.cn

Abstract. Recent research data and evidence from multiple societies demonstrated that men's health problems have become increasingly worse than women around the world. A World Health Organization (WHO) report published recently described a significant gender gap in life expectancy that, in some regions the average life expectancy for men is 5.1 years less than for women. The primary causes of male premature mortality are cardiovascular disease, cancer, diabetes, and chronic respiratory diseases. The main risk factors for the aforementioned diseases, are caused by some bad lifestyle habits such as smoking, wine consumption, sedentary, counterbalanced diet, seldom exercise, irregular sleep and etc. Genetic factors are also known to play an important role in people's health, and much work has been done to identify the genes related specifically to men's health, such as the genes related to homocysteine level, alcohol metabolism ability, nicotine dependence, prostate specific antigen level, and so on. In this paper, we first describe the genetic risk factors that affect men's health, then we demonstrate the implementation of a personalized nutrition service specially designed for men based on men's genetic factors and lifestyles. The personalized nutrition service provides genetic testing, lifestyle assessment, personalized nutrition solution, and personalized nutritional supplements production, so that to improve men's health effectively.

Keywords: Men's health · Personalized nutrition · Genetic testing · Personalized solution

1 Introduction

In recent years, statistics found that men's health problems have become growing prominent in many countries. A recent World Health Organization (WHO) report [1] shows that, in some areas of the world the average life expectancy is 5.1 years less for men than for women [2]. The main causes of male death are cardiovascular disease, cancer, diabetes, and chronic respiratory diseases, which are caused by genetic factors and bad lifestyle habits. The bad lifestyle habits such as smoking, wine drinking, sedentary, counterbalanced diet, seldom exercise, and irregular sleep, are more prevalent among men than women. Therefore,

© Springer Nature Switzerland AG 2021
O. Gervasi et al. (Eds.): ICCSA 2021, LNCS 12957, pp. 195–204, 2021.
https://doi.org/10.1007/978-3-030-87013-3_15

it's necessary to design and implement a tailored personalized nutrition service for men's health.

2 Related Work

There are some data analysis [3,4] and models [5] in men's health, which analyzes and summarizes the factors affecting men's health, however most of the solutions for improving men's health are generic, and there are a lack of attempts to design and implement personalized solutions (especially based on genetic factors) to improve men's health specifically. Therefore, in this paper, we consider improving men's health from both genetic and lifestyle aspects, analyze multiple dimensional data and calculate personalized nutrition solution, as well as produce personalized nutrition product for each person to improve men's health effectively.

3 Genetic Factors and Men's Health

Many genes have associations with men's health considering men's unhealthy lifestyles, for example (just to name a few) the homocysteine level, alcohol metabolism, nicotine dependence, and prostate specific antigen (PSA) level are all affected by genes.

3.1 Homocysteine Level

Folic acid deficiency and elevated homocysteine (Hcy) levels are considered risk factors for many diseases, such as hypertension, stroke, and male infertility. Methylenetetrahydrofolate reductase (MTHFR) is a key enzyme in folate metabolism. The mutant genotype is closely related to decreased enzyme activity, as a result, the availability of folic acid is severely reduced, and the level of Hcy is significantly increased, which brings serious risks of diseases [6].

The results of meta-analysis suggest that blood Hcy is significantly related to the risk of stroke and coronary heart disease [8]. The level of folic acid will also affects the process of sperm production and probably reduces male fertility [9]. Individuals having TT genotype of MTHFR C677T will probably have significantly higher blood pressure risk than those having CC genotype [7].

3.2 Alcohol Metabolism

Alcohol consumption, a lifestyle much more popular in men than in women, is a relevant risk factor for atherosclerotic diseases, such as hypertension, dyslipidemia, and obesity. Different people's ability in alcohol consumption are partially decided by genetic factors. Aldehyde dehydrogenase is an important enzyme in alcohol metabolism, the Aldehyde dehydrogenase 2 (ALDH2) gene's mutation will greatly reduce the activity of the aldehyde dehydrogenase enzyme, which will result in a large accumulation of acetaldehyde [10].

The mutation of ALDH2*2 has an important impact on human health [11], the polymorphism of ALDH2 rs671 has been found to be an established genetic risk for coronary heart diseases and hypertension in Asian population [12].

3.3 Nicotine Dependence

Cigarette smoking is a leading contributor to men's disease and death, causing approximately five million premature deaths each year around the world. Cigarette smoking is a primary cause of lung cancer, and one of the major risk factors causing peripheral arterial disease. Genetic factors have been found to contribute to the development of nicotine dependence [13,15], some evidences for genetic influence on smoking behavior have also been identified [14].

3.4 Prostate Specific Antigen Levels

In some countries, prostate cancer is the most frequent cancer in men, prostate specific antigen (PSA) levels in the general population is also affected by inherited factors [16].

The mutation of rs17632542 in KLK3 was found to affect PSA levels [17], and this variant has a stronger effect on PSA levels than the variant of rs2735839 previously reported [18].

4 Personalized Nutrition Service for Men's Health

A personalized nutrition service for men's health includes four parts:

- genetic testing,
- lifestyle assessment,
- personalized nutrition solution, and
- personalized nutritional supplements product.

4.1 Genetic Testing

As shown in Fig. 1, a Men's Health Genetic Testing Report has four modules:

- Men's Health (in Fig. 1 left), which includes the testing items of: Male Pattern Baldness, Prostate-specific Antigen Level Elevation, Benign Prostatic Hyperplasia, Serum Testosterone Concentrations in Men, Norepinephrine and Epinephrine Concentrations at Rest and After Exercise, SSRI/SNRI-induced Sexual Dysfunction, Orepinephrine and Epinephrine Concentrations at Rest and After Exercise;
- Liver Protection, which includes the testing items of: Alcohol Dependence, Alcohol Consumption, Alcoholic Fatty Liver, Alcohol-related Cirrhosis, Inflammatory Bowel Disease, Duodenal Ulcer;

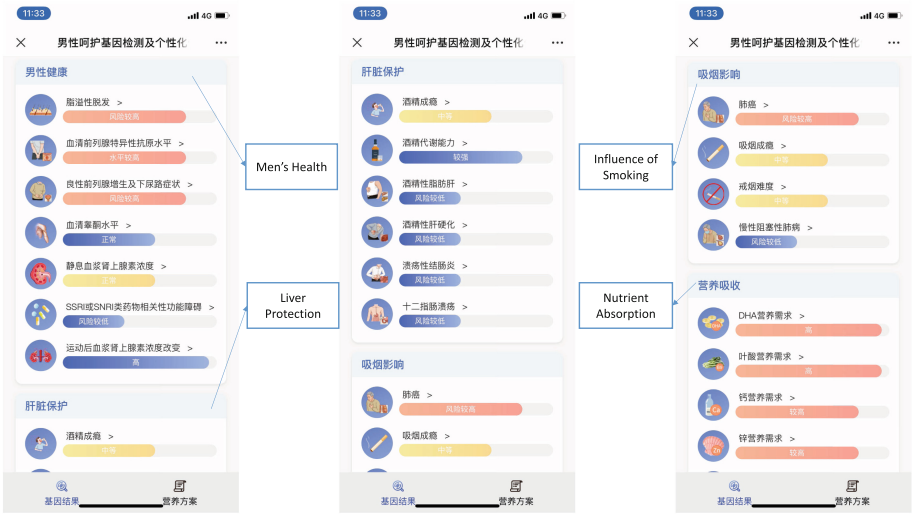

Fig. 1. The screen shots of the user interface (first level) of the Men's Health Genetic Testing Report.

- Influence of Smoking (in Fig. 1 right), which includes the testing items of: Lung Cancer, Nicotine Dependence, Etiology of Tobacco, Chronic Obstructive Pulmonary Disease; and
- Nutrient Absorption, which tests the nutritional requirement items of: DHA, Folate, Vitamin D, Zinc, Vitamin A, Vitamin E, Vitamin B1, Vitamin B2, Vitamin B6, Vitamin C, Magnesium, Selenium, Lycopene, Vitamin B12.

The men's health genetic testing report was implemented in Java web application using spring boot [19] and mybatis [20] framework, and the users can access the report both in personal computer and mobile phones. By clicking the name of each genetic testing item, a detail testing result report will be opened as described in Fig. 2.

Using the genetic testing item of Nicotine Dependence as an example, Fig. 2 demonstrates the screen shots of the user interface of a testing item. Each testing item report includes six parts:

- testing item name and its testing result (*e.g.*, Nicotine Dependence in Fig. 2 left, risk level: medium), which gives the testing result and the population gene frequency, explains the testing result, as well as provides some health advice based on the testing result;
- testing item introduction, which explains the testing contents of the item and emphasizes the importance of the testing item;
- testing item analysis (*e.g.*, Harms of Smoking), explains the relationship between the testing item and the health of a person, and analyzes why it is necessary to test the item;



Fig. 2. The screen shots of the user interface (second level) of the Men's Health Genetic Testing Report.

- the tested gene loci and genotype (*e.g.*, *CHRNA3* in Fig. 2 middle), lists the tested genes and loci and the corresponding genotypes;
- gene analysis (in Fig. 2 right) for the tested genes, explains the association between the genes and the testing item, for example explaining the association between the genes *CHRNA, CTNNA3* and nicotine dependence; and
- scientific references, list the scientific research papers and clinical evidences for the testing item.

4.2 Lifestyle Assessment

Not only the genetic factors affect men's health, the lifestyle also plays a very important role for men's health, such as smoking, wine drinking, sedentary, irregular sleep, obesity and etc. Therefore, we implemented a food frequency questionnaire (FFQ) [21–23] to assess a person's lifestyle.

4.3 Personalized Nutrition Solution

Based on the genetic testing results and food frequency questionnaire, the personalized nutrition service platform will calculate a personalized nutrition solution for each customer, the screen shots of the personalized nutrition report are described in Fig. 3. The personalized nutrition report includes three parts:

- daily personalized nutrition solution (in Fig. 3 left), which lists the recommended nutrition supplements, click each icon of the tablets, more detail information about the tablet will be shown describing the product information such as ingredients, subsidiary material, directions and dosage, and etc.;



Fig. 3. The screen shots of the user interface of the personalized nutrition solution.

– nutrition facts, which list all the nutrient content (such as Vitamin C, 60 mg) in the daily personalized nutrition solution;
– core nutrition supplement (in Fig. 3 middle), explains why the suggested nutritional supplements are beneficial for the user, click each item, nutrient analysis will be displayed in a dropdownlist (in Fig. 3 right) to explain why the nutrient is recommended, including the functions of the nutrient, evaluation and suggestions, and food sources.

4.4 Personalized Nutritional Supplements Production

According to the personalized nutrition solution, the user can place an order to the nutrition factory to produce a monthly personalized nutrition box product including 30 daily nutrition packs. Each customer's name and the information of the tablets (inside the nutrition pack) will be printed on the pack, which means each customer will have a unique nutrition box.

The personalized nutrition box production requires nutrition factory to have the flexible manufacturing capability, which is a challenge for the traditional standardized production factory.

Figure 4 demonstrates the personalized nutrition box production process from order to delivery, in which multiple departments are involved in, such as Sales, Planning, Purchase, Workshop, Warehouse, Quality control, and Finance. Comparing to the standardized production pipeline that produces tens of thousands of exactly the same products at a time, the personalized production pipeline is much more complicated that each customer has a unique product composition with small production amount (such as 30 packs for one month per person, 90 packs for three months per person). Therefore, all the production process should

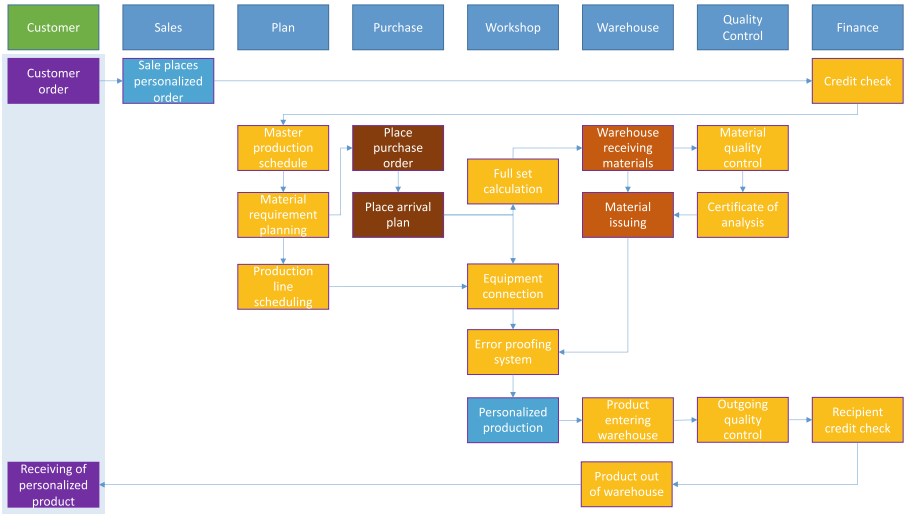

Fig. 4. The supply chain (from order to delivery) for personalized nutrition product production.

be digitalized so that to promote production efficiency as well as reduce or avoid production errors.

5 Conclusions

Men's health problem is partially caused by bad lifestyle habits, such as smoking, wine drinking, sedentary, counterbalanced diet, seldom exercise, and irregular sleep. Men's health is also closely related to genetic factors, for instance, the MTHFR genetic polymorphism can assess an individual's ability for folic acid metabolism, the ALDH2 gene can be tested to evaluate a person's ability for alcohol metabolism, the CHRNA4 gene can be used to assess a person's nicotine dependence tendency.

Combining both the genetic testing data and lifestyle data, in this paper, we design and implement a tailored personalized nutrition service for men's health. The service requires the user to have a genetic testing, as well as finish online lifestyle assessment questionnaires, then the system will analyze both the genetic data and the lifestyle data together, using the genetic interpretation database (such as the Online Catalog of Human Genes and Genetic Disorders (OMIM) [24,25], the AutDB [26]) and the scientific evidences [27–35] to calculate a genetic report and a personalized nutrition solution report, respectively. Based on the personalized nutrition solution, the nutrition factory will produce a monthly personalized nutrition box product for the customer. A personalized lifestyle solution will also be given to the customer. The personalized nutrition service for men has been delivered online, and has been used by tens of thousands of customers.

Concerning future work, we will combine more dynamic data such as sports data [36], physical examination data and sleep data to our data model to further perfect our service for men's health.

Acknowledgment. This research project is supported by Science Foundation of Beijing Language and Culture University (supported by "the Fundamental Research Funds for the Central Universities") (Approval number: 21YJ040002).

References

1. Rodrigues, R., Ilinca, S., Kai, L., et al.: The health and well-being of men in the WHO European Region: better health through a gender approach (2018). https://www.euro.who.int/en/publications/abstracts/the-health-and-well-being-of-men-in-the-who-european-region-better-health-through-a-gender-approach-2018. Accessed 29 Apr 2021
2. GBD 2017 Mortality Collaborators: Global, regional, and national age-sex-specific mortality and life expectancy, 1950–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet **392**, 1684–1735 (2018)
3. Rajaratnam, J.K., et al.: Worldwide mortality in men and women aged 15–59 years from 1970 to 2010: a systematic analysis. Lancet **375**, 1704–1720 (2010)
4. Wang, H., et al.: Age-specific and sex-specific mortality in 187 countries, 1970–2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet **380**, 2071–2094 (2012)
5. Ashraf, K., Ng, C.J., Goh, K.L.: Theories, models and frameworks in men's health studies: a scoping review. J. Men's Health **17**(2), 15–24 (2021)
6. Ueland, P.M., Hustad, S., Schneede, J., et al.: Biological and clinical implications of the MTHFR C677T polymorphism. Trends Pharmacol. Sci. **22**(4), 195–201 (2001)
7. Saraswathy, K.N., Garg, P.R., Salam, K., et al.: MTHFR C677T polymorphism and its homocysteine-driven effect on blood pressure. Int. J. Stroke **9**(4), E20 (2014). Official Journal of the International Stroke Society
8. Holmes, M.V., Newcombe, P., Hubacek, J.A., et al.: Effect modification by population dietary folate on the association between MTHFR genotype, homocysteine, and stroke risk: a meta-analysis of genetic studies and randomised trials. Lancet **378**(9791), 584–594 (2011)
9. Gong, M., Dong, W., He, T., et al.: MTHFR 677C>T polymorphism increases the male infertility risk: a meta-analysis involving 26 studies. PLOS ONE **10**(3), e0121147 (2015)
10. Takeuchi, F., Isono, M., Nabika, T., et al.: Confirmation of ALDH2 as a Major locus of drinking behavior and of its variants regulating multiple metabolic phenotypes in a Japanese population. Circ. J. **75**(4), 911–918 (2011). Official Journal of the Japanese Circulation Society
11. Wang, L., Wu, Z.: ALDH2 and cancer therapy. Adv. Exp. Med. Biol. **1193**, 221–228 (2019)
12. Xia, C.L., Chu, P., Liu, Y.X., et al.: ALDH2 rs671 polymorphism and the risk of heart failure with preserved ejection fraction (HFpEF) in patients with cardiovascular diseases. J. Hum. Hypertens **34**(1), 16–23 (2020)
13. Carmelli, D., Swan, G.E., Robinette, D., et al.: Genetic influence on smoking-a study of male twins. N. Engl. J. Med. **327**(12), 829–833 (1992)

14. Thorgeirsson, T.E., Geller, F., Sulem, P., et al.: A variant associated with nicotine dependence, lung cancer and peripheral arterial disease. Nature **452**(7187), 638–642 (2008)
15. Bierut, L.J., Madden, P.A., Breslau, N., et al.: Novel genes identified in a high-density genome wide association study for nicotine dependence. Hum. Mol. Genet. **16**(1), 24–35 (2007)
16. Barry, M.J.: Screening for prostate cancer-the controversy that refuses to die. N. Engl. J. Med. **360**(13), 1351–1354 (2009)
17. Gudmundsson, J., Besenbacher, S., Sulem, P., et al.: Genetic correction of PSA values using sequence variants associated with PSA levels. Sci. Transl. Med. **2**(62), 62ra92 (2010)
18. Eeles, R.A., Kote-Jarai, Z., Giles, G.G., et al.: Multiple newly identified loci associated with prostate cancer susceptibility. Nat. Genet. **40**(3), 316–321 (2008)
19. Spring Boot. https://spring.io/projects/spring-boot/. Accessed 29 Apr 2021
20. MyBatis. https://mybatis.org/mybatis-3/index.html. Accessed 29 Apr 2021
21. Johns, R., Kusuma, J., Lie, A., Shiao, S.P.K.: Validation of macro- and micronutrients including methyl donors in social ethnic diets using food frequency questionnaire and nutrition data system for research (USDA computerized program). SDRP J. Food Sci. Technol. **3**(4), 417–430 (2018)
22. Affret, A., El Fatouhi, D., Dow, C., Correia, E., Boutron-Ruault, M.C., Fagherazzi, G.: Relative validity and reproducibility of a new 44-item diet and food frequency questionnaire among adults: online assessment. J. Med. Internet. Res. **20**(7), e227 (2018)
23. Thompson, F.E., Subar, A.F.: Chapter 1 - Dietary assessment methodology. In: Nutrition in the Prevention and Treatment of Disease, 4th edn. Academic Press (2017). ISBN 9780128029282
24. Hamosh, A., Scott, A.F., Amberger, J.S., Bocchini, C.A., McKusick, V.A.: Online Mendelian Inheritance in Man (OMIM), a knowledgebase of human genes and genetic disorders. Nucleic Acids Res. **33**(Database issue), D514–D517 (2005)
25. OMIM - Online Mendelian Inheritance in Man, an Online Catalog of Human Genes and Genetic Disorders. https://www.omim.org/. Accessed 20 May 2021
26. Pereanu, W., et al.: AutDB: a platform to decode the genetic architecture of autism. Nucleic Acids Res. **46**(D1), D1049–D1054 (2018)
27. Corella, D., Ordovas, J.M.: Nutrigenomics in cardiovascular medicine. Circ. Cardiovasc. Genet. **2**, 637–651 (2009)
28. Frazier-Wood, A.C.: Dietary patterns, genes, and health: challenges and obstacles to be overcome. Curr. Nutr. Rep. **4**, 82–87 (2015)
29. Vallee Marcotte, B.V., et al.: Novel genetic loci associated with the plasma triglyceride response to an omega-3 fatty acid supplementation. J. Nutrigenet. Nutrigenomics **9**, 1–11 (2016)
30. Ouellette, C., Rudkowska, I., Lemieux, S., Lamarche, B., Couture, P., Vohl, M.C.: Gene-diet interactions with polymorphisms of the MGLL gene on plasma low-density lipoprotein cholesterol and size following an omega-3 polyunsaturated fatty acid supplementation: a clinical trial. Lipids Health Dis. **13**, 86 (2014)
31. Rudkowska, I., et al.: Interaction between common genetic variants and total fat intake on low-density lipoprotein peak particle diameter: a genome-wide association study. J. Nutrigenet. Nutrigenomics **8**, 44–53 (2015)
32. Tremblay, B.L., Cormier, H., Rudkowska, I., Lemieux, S., Couture, P., Vohl, M.C.: Association between polymorphisms in phospholipase A2 genes and the plasma triglyceride response to an N-3 PUFA supplementation: a clinical trial. Lipids Health Dis. **14**, 12 (2015)

33. Palatini, P., et al.: CYP1A2 genotype modifies the association between coffee intake and the risk of hypertension. J. Hypertens. **27**, 1594–1601 (2009)
34. De Toro-Martin, J., Arsenault, B.J., Despres, J.P., Vohl, M.C.: Precision nutrition: a review of personalized nutritional approaches for the prevention and management of metabolic syndrome. Nutrients **9**(8), pii:E913 (2017)
35. Grimaldi, K.A., van Ommen, B., Ordovas, J.M., et al.: Proposed guidelines to evaluate scientific validity and evidence for genotype-based dietary advice. Genes Nutr. **12**, 35 (2017)
36. Patel, M.S., Asch, D.A., Volpp, K.G.: Wearable devices as facilitators, not drivers, of health behavior change. JAMA **313**, 459–460 (2015)