

Classical and potential risk factors of cardiovascular disease among Chinese patients with type 2 diabetes mellitus: a cross-sectional study based on Framingham 10-year general cardiovascular disease risk score

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Abstract

Background : Cardiovascular risk is greatly increased in diabetic patients, and more than 70% of diabetic patients die of cardiovascular disease. Unfortunately, in China, the awareness rate, treatment rate, and control rate of cardiovascular risk in diabetic patients are still far from enough. Identifying and managing cardiovascular disease risk in T2DM patients is particularly important through relevant risk factor management tools. **Methods:** In this study, 750 patients with type 2 diabetes were selected from a Grade-A Tertiary Hospital(beds>500)in Harbin, the response rate was 93.6%. We collected general demographic data, dietary status, and laboratory tests for patients, selected NEO Five-Factor Inventory for personality assessment, and used the Framingham 10-year general cardiovascular disease risk score(FRS) . Statistical analysis includes one-way ANOVA,chi-square analysis,Spearman correlation analysis, univariate and multiple regression analysis. **Results:** 291 people in the low-risk group, 239 in the Mid-risk group and 172 in the High-risk group. FRS was correlated with Age, SBP, DBP , Duration, TC, LDL-C, TC, regular diet, spicy food intake and open personality **Conclusions:** In addition to traditional risk factors, diet and personality may also should be included for cardiovascular disease in people with type 2 diabetes. **Key words:** China T2DM cardiovascular disease

Background

Type 2 diabetes (T2DM) is a progressive disease characterized by progressive loss of insulin resistance and b-cell function leading to insulin deficiency. This disease accounts for 95% of all cases of diabetes [1], and if left uncontrolled, can lead to severe long-term morbidity, various acute and chronic complications and early death [2].

Among them, cardiovascular and cerebrovascular complications are the most dangerous, which has seriously threatened the health and life of patients with type 2 diabetes. Studies have shown that diabetes is an established risk factor for coronary heart disease and ischemic stroke [3, 4]. Studies have shown that cardiovascular risk is greatly increased in diabetic patients, and more than 70% of diabetic patients die of cardiovascular disease. In addition, Asians are more likely to develop cardiovascular complications of diabetes due to more visceral fat accumulation [5]. The study found that cardiovascular disease as a major complication of diabetes patients is the leading cause of death in diabetic patients [6]. Unfortunately, in China, the awareness rate, treatment rate, and control rate of cardiovascular risk in diabetic patients are still far from enough [7, 8]. There are still some doctors, especially those in primary hospitals, who are under-recognized and under-managed for the risk of cardiovascular disease in patients with type 2 diabetes. This poses a huge challenge to the prevention and control of CVD diseases in diabetic patients.

Identifying and managing CVD risk in T2DM patients is particularly important through relevant risk factor management tools.The study found that every 1 standard deviation of LDL-C, non-HDL-C and apoB in blood lipids the risk of cardiovascular events increased by 1.13 (95% CI, 1.10–1.17), 1.16 (95% CI, 1.12–1.19) and 1.14 (95% CI, 1.11–1.18) [9]. It can be seen that if timely and effective intervention is not

carried out on relevant risk factors, Then the risk of cardiovascular events is significantly increased. In addition, an analysis from the UK database shows that to reduce the risk of cardiovascular and cerebrovascular diseases in diabetic patients, the focus is on prevention [10].

ATPIII and other guidelines [11–14] recommend five-year and ten-year risk assessments, some of which are based on the multivariate regression equation of the Framingham cohort, which was created in 1948 by the Framingham Institute of the United States. According to the risk factors, the scores of males and females were obtained, and the scores were converted into the probability of cardiovascular events within a certain period of time. The main research factors of Framingham's 10-year framingham risk score (FRS) are gender, age, diabetes, systolic blood pressure, diastolic blood pressure, smoking history, TC, HDL-C, and LDL-C, which are recommended by NCEP-ATP III. The scoring tool is one of the most widely used scoring tools for assessing the risk of coronary heart disease in individuals over the next 10 years [15, 16]. FRS has proven to be a good predictor of cardiovascular disease risk [17, 18]. FRS has also been applied to Asian populations and has become an effective method to predict the 10-year risk of general cardiovascular disease in this population [19, 20].

This risk model contains only physiological factors. It is well known that non-communicable diseases such as diabetes (DM) and cardiovascular disease (CVD) are closely related to psychosocial factors and behavioral patterns. Unhealthy lifestyles and unreasonable eating habits drive the development of chronic diseases [21, 22]. In clinical practice and research, the relationship between personality and cardiovascular disease has also been extensively explored. Study found that inhibition of emotional and psychological risk factors is associated with coronary adverse events [23]. To predict the development of cardiovascular adverse events in patients with type 2 diabetes, dietary and psychological factors should be considered to supplement the traditional cardiovascular risk model.

To further explore the application of the FRS in China, and its classical and potential risk factors, we conducted a cross-sectional survey in an A grade hospital in Heilongjiang Province. In order to understand the possibility of cardiovascular disease and related physiological, psychological and behavioral factors in patients with type 2 diabetes. Strengthen the attention and prevention of cardiovascular complications by medical staff and patients to ensure the prognosis and health of patients.

Methods

Study design and participants

In this study, 750 patients with type 2 diabetes were selected from a Grade-A Tertiary Hospital (beds > 500) in Harbin by means of convenient sampling, excluding patients with cardiovascular disease or other cognitive impairment. 750 people with diabetes participated our research. The purpose and significance of our research were explained clearly as well as method by which to complete the questionnaires. Participation was completely voluntary and anonymous, without economic interests. Each participant signed an informed consent. We provided an immediate explanation to ensure that there are no unclear

questionnaire items. Self-administered questionnaires were distributed directly to participants who were requested to complete questionnaires in 15 min. We collected and checked the questionnaires immediately after completion. The quality of our research can be ensured. All questionnaires were collected but there are 48 invalid questionnaires were excluded (the response rate was 93.6%). This study was approved by the Ethics Committee of Harbin Medical University.

Measures

We collected general demographic data, dietary status, and laboratory tests for patients, selected NEO Five-Factor Inventory (NEO-FFI) for personality assessment, and used the Framingham 10-year general cardiovascular disease risk score (FRS) to evaluate patients with heart disease over the next 10 years. risk. General demographic data include: gender, age, family location, marital status, cultural level, smoking, etc. Dietary conditions include: eating habits, sweet taste preferences, salt intake, and spicy food intake. Laboratory tests include: BMI index, systolic blood pressure, diastolic blood pressure, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol.

Framingham 10-year general cardiovascular disease risk score

Framingham 10-year general cardiovascular disease risk score (FRS) comes from the Framingham Heart Study, a scoring system that includes traditional risk factors (age, total cholesterol, high-density lipoprotein cholesterol, systolic blood pressure, smoking status), etc. Risk factors were scored for men and women, respectively, and the score was converted to the probability of a cardiovascular event within a certain period of time. The FRS is a NCEP-ATP III recommended scoring tool and is one of the most widely used scoring tools for assessing the risk of coronary heart disease in individuals over the next 10 years [15-16]. According to 10 Yr CHD Risk, the FRS score was obtained. The subjects were divided into Low-risk group (FRS < 10%), Mid-risk group (10% ≤ FRS < 20%) and High-risk group (FRS ≥ 20%).

NEO Five-Factor Inventory (NEO-FFI)

NEO Five-Factor Inventory (NEO-FFI) is based on the Big Five personality theory, compiled by the American psychologists Costa and Macrae in 1987, and later revised twice, the Chinese version of the test. Revised by Professor Zhang Jianxin [24], a psychologist at the Chinese Academy of Sciences, is a personality test tool for the genre of personality theory. We selected the 25-question Big Five Personality Questionnaire, which is divided into five dimensions, including adaptability (1, 6, 11, 16, 21 questions), social (2, 7, 12, 17, 22 questions). Openness (3, 8, 13, 18, 23 questions), altruism (4, 9, 14, 19, 24 questions), moral sense (5, 10, 15, 20, 25 questions). According to the Big Five Personality Factor Score Conversion Table, the scores and corresponding explanations for each dimension can be obtained.

Statistical analysis

Data analysis was performed using SPSS 19.0 statistical software. One-Way ANOVA was used to compare the measurement data among different risk groups, and the χ^2 test was used for the count data;

the correlation between the possible influencing factors and the risk group was analyzed by Spearman correlation analysis, Univariate and multivariate regression analysis tests the risk factors for FRS.

Results

One-way ANOVA and chi-square analysis results

Baseline characteristics of 702 subjects are shown in Table 1. In the overall sample of the study, 291 people in the low-risk group, accounting for 41.5%, 239 in the Mid-risk group, accounting for 34.0%, and 172 in the High-risk group, accounting for 24.5%. There was no significant difference in the ratio of male to female between the three groups ($P > 0.05$). The mean ages of the low-risk, Mid-risk and High-risk groups were 39.46 ± 12.826 , 55.15 ± 10.117 and 62.97 ± 8.120 years, respectively ($P < 0.001$). Among the three different risk groups, the composition ratios of SBP, DBP, HDL-C, LDL-C, and HBA1C were statistically different. There was no statistical difference between the BMI index and smoking status among the three groups. In addition, there were statistically significant differences between the different risk groups in terms of marital status, family location, education, eating habits, and spicy dietary intake.

Spearman correlation analysis

Spearman correlation analysis found that FRS was positively correlated with Age, SBP, DBP, Duration, TC, LDL-C, TC, regular diet, and spicy food intake, and negatively correlated with open personality (all $P < 0.05$).

Univariate and multivariate regression analysis

Using FRS as the dependent variable (0 = Low-risk or Mid-risk, 1 = High-risk), using single factor and multiple Factor logistics Regression analysis Risk factors for High-risk. Univariate analysis results show that age SBP, DBP, TC, and LDL-C are risk factors for High-risk. Open personality, spicy diet, and regular diet are protective factors for high-risk groups. Further multivariate analysis of regression analysis showed that high age, high blood pressure, and LDL-C were independent risk factors for High-risk. (Table 4)

Table 1
One-way ANOVA analysis of different risk groups

| Variables | low-risk | middle-risk | high-risk | f | P |
|------------------|-----------------|--------------------|------------------|----------|----------|
| age | 39.46 ± 12.826 | 55.15 ± 10.117 | 62.97 ± 8.120 | 282.338 | 0.000 |
| BMI | 25.51 ± 4.50 | 25.59 ± 3.82 | 25.99 ± 3.61 | 0.808 | 0.446 |
| SBP | 127.11 ± 16.039 | 136.03 ± 18.056 | 149.0 ± 18.625 | 86.157 | 0.000 |
| DBP | 81.92 ± 11.162 | 85.07 ± 12.055 | 86.23 ± 11.567 | 8.9 | 0.000 |
| HDL-C | 1.22 ± 0.39 | 1.24 ± 0.32 | 1.15 ± 0.26 | 3.494 | 0.031 |
| LDL-C | 2.60 ± 0.75 | 2.88 ± 1.03673 | 3.26 ± 1.60 | 19.119 | 0.000 |
| TC | 4.586 ± 1.023 | 4.889 ± 1.175 | 5.159 ± 1.132 | 15.124 | 0.000 |
| Hba1c | 9.117 ± 2.145 | 8.615 ± 1.959 | 8.936 ± 1.964 | 3.629 | 0.027 |
| personality | 50.37 ± 9.78 | 49.49 ± 10.23 | 47.88 ± 9.45 | 3.441 | 0.033 |

Table 2
Chi-square analysis of different risk groups

| Variables | low-risk | middle-risk | high-risk | χ^2 | P |
|---------------------------|-----------------|--------------------|------------------|----------------------------|----------|
| Gender | | | | | |
| Male | 182 | 141 | 102 | 0.838 ^a | 0.658 |
| Female | 109 | 98 | 70 | | |
| marital status | | | | | |
| unmarried | 47 | 4 | 0 | 70.573 ^a | 0.000 |
| married | 232 | 219 | 160 | | |
| Divorced | 10 | 5 | 2 | | |
| Widowed | 2 | 11 | 1 | | |
| Region | | | | | |
| city | 128 | 137 | 102 | 15.770 ^a | 0.003 |
| county seat | 105 | 74 | 46 | | |
| rural | 58 | 28 | 24 | | |
| Education | | | | | |
| Elementary school | 22 | 29 | 28 | 19.578 ^a | 0.012 |
| junior high school | 106 | 62 | 55 | | |
| High school | 72 | 74 | 46 | | |
| Bachelor | 82 | 68 | 43 | | |
| Master degree and above | 9 | 6 | 0 | | |
| Smoking status | | | | | |
| smoker | 41 | 47 | 35 | 4.083 ^a | 0.130 |
| Non-smoker | 250 | 192 | 137 | | |
| Diet | | | | | |
| Unquantized | 126 | 66 | 39 | 35.365 | 0.000 |
| Untimed quantification | 34 | 20 | 17 | | |
| Timing but not quantified | 74 | 88 | 54 | | |

| Variables | low-risk | middle-risk | high-risk | χ^2 | P |
|---------------------------|-----------------|--------------------|------------------|----------------------------|----------|
| Timing and quantification | 57 | 65 | 62 | | |
| Do you like sweets | | | | | |
| Like | 174 | 138 | 93 | 1.451 ^a | 0.484 |
| Dislike | 117 | 101 | 79 | | |
| Salt intake | | | | | |
| very heavy | 11 | 14 | 4 | 6.974 ^a | 0.323 |
| Partial | 169 | 128 | 106 | | |
| Poor | 102 | 88 | 60 | | |
| Very light | 9 | 9 | 2 | | |
| Spicy food intake | | | | | |
| Always | 77 | 40 | 26 | 18.601 ^a | 0.005 |
| Often | 91 | 81 | 47 | | |
| Sometimes | 88 | 81 | 61 | | |
| Never | 35 | 37 | 38 | | |

Table 3
Spearman correlation analysis

| Variables | R | P |
|------------------|----------|----------|
| Gender | 0.284 | 0.420 |
| age | 0.695 | 0.000** |
| BMI | 0.069 | 0.067 |
| SBP | 0.441 | 0.000** |
| DBP | 0.150 | 0.000** |
| LDL-C | 0.264 | 0.000** |
| HDL-C | -0.064 | 0.088 |
| Smoke | 0.072 | 0.056 |
| HAB1C | -0.043 | 0.284 |
| TC | 0.219 | 0.000** |
| marital status | 0.235 | 0.000** |
| Region | -0.134 | 0.000** |
| Education | -0.063 | 0.094 |
| Sweet | 0.043 | 0.238 |
| Spicy | 0.148 | 0.000** |
| Salt | -0.010 | 0.801 |
| Diet | 0.206 | 0.000** |
| personality | -0.124 | 0.001** |

Table 4
Univariate and multivariate regression analysis

| Variables | Univariate | | multivariate | |
|--|------------|-------|--------------|-------|
| | OR | P | OR | P |
| age | 1.131 | 0.000 | 1.160 | 0.000 |
| SBP | 1.054 | 0.000 | 1.047 | 0.000 |
| DBP | 1.021 | 0.005 | 1.020 | 0.114 |
| LDL-C | 1.685 | 0.000 | 1.956 | 0.000 |
| TC | 1.398 | 0.000 | 1.093 | 0.512 |
| marital status | | | | |
| Unmarried- married | 0.000 | 0.997 | | |
| Divorced - married | 0.376 | 0.197 | | |
| Widowed-married | 2.168 | 0.072 | | |
| Region | | | | |
| City-rural | 1.379 | 0.241 | | |
| Country side-rural | 0.921 | 0.722 | | |
| Spicy intake | | | | |
| Always-never | 0.421 | 0.003 | 1.555 | 0.307 |
| Often-never | 0.518 | 0.011 | 0.796 | 0.522 |
| Sometimes-never | 0.684 | 0.129 | 0.895 | 0.746 |
| Diet | | | | |
| Unquantized-Timing and quantification | 0.400 | 0.000 | | 0.385 |
| Untimed quantification - Timing and quantification | 0.619 | 0.133 | | 0.294 |
| Timing but not quantified -Timing and quantification | 0.656 | 0.057 | | 0.910 |
| personality | 0.975 | 0.004 | 0.984 | 0.189 |

Discussion

In our study, 291 people in the low-risk group, accounting for 41.5%, 239 in the Mid-risk group, accounting for 34.0%, and 172 in the High-risk group, accounting for 24.5%. The age of onset of each risk group is

significantly lower than other studies[25, 26]. This suggests that the risk of cardiovascular complications in patients with T2DM is not optimistic, and it is imperative to control and manage related risk factors.

The Framingham model is one of many tools for predicting the risk of cardiovascular disease, it has been widely used around the world and is the most classic evaluation tool[27, 28]. However, the application of this risk model for European white samples to the Chinese population still needs to be improved. It has been found that the use of the FRS model in Asian populations may result in a lower risk[29]. Our study explored the traditional risk factors of the FRS model and found that there was no statistically significant difference in gender, smoking, and HDL-C among our traditional risk factors. The role of hypotension as a risk factor in multivariate logistic regression was also offset. We conducted a multivariate logistic regression analysis of high-risk group and low-risk groups. The most important risk factors were age, hypertension, and low-density lipoprotein cholesterol.

In addition, we further considered the impact of dietary preferences on cardiovascular risk factors in diabetic patients. In terms of diet, we independently designed issues related to dietary habits and dietary preferences, including regular diet, sweetness, salt and spicy. Food preferences. The protective effect of timed quantitative diet on cardiovascular disease is self-evident, especially in this group of patients with type 2 diabetes. However, it is interesting to note that the protective effect of spicy dietary preferences on cardiovascular disease has caught our attention. The traditional view has always been to avoid patients with a spicy diet to protect cardiovascular disease[30], but our research has reached the opposite conclusion, a British study[31] and we came to a similar conclusion. It found that a spicy diet as part of a daily diet can reduce the risk of death. Previous studies[32, 33] have shown that the beneficial effects of spices and their bioactive ingredients such as capsaicin include anti-obesity, anti-oxidant, anti-inflammatory and anti-cancer properties. Although our cross-sectional study does not give such a conclusion, it also suggests that we may have to re-examine our dietary standards.

The discussion between the relationship between personality factors and cardiovascular disease can be said to be a hot topic[34–36]. Our study found that open personality can be used as a protective factor for the risk of cardiovascular disease in diabetic patients. The study found that emotional inhibition can make individuals unable to successfully adapt to stress events. Repeatedly, it will form a long-term stress state, which will adversely affect the normal function of the cardiovascular system. In contrast, open personality compares curious, novel, unconventional, and creative individuals with those who are traditional, uninterested, and non-analytical. Open people prefer abstract thinking and have a wide range of interests. These qualities may have contributed to their protection from cardiovascular disease.

Although psychological behavioral factors have less effects on cardiovascular disease than age, blood pressure, low-density lipoprotein cholesterol, etc., we should not stop exploring and discussing them. The role of psychological behavior factors in this model is easily offset. Or show a less effective result. However, considering that the model itself is composed of these physiological factors, psychological factors and behavioral factors should be considered even if they are weak. And further exploration in the longitudinal study.

Limitations

There are several limitations in our research. The first limitation is the possibility of sampling bias, the subjects of our study come from one hospital in Heilongjiang Province, it may not represent all adults with T2DM. The second limitation is that cross-sectional studies involve weak causal inferences. Therefore, future researches should include a longitudinal follow-up to determine the mediating effects.

Conclusions

In addition to traditional risk factors, diet and personality may also should be included for cardiovascular disease in people with type 2 diabetes.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Harbin Medical University.

Consent for publication

Each participant signed an informed consent in our study.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors claim that there are no conflicts of interest. We do not hold any stocks or shares in an organization that may in any way gain or lose financially from the publication of this manuscript, either now or in the future.

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Authors' contributions

Conceived and designed the experiments: YJY HP

Data collection: YX XJS

Analyzed the data: TYZ XJS

Contributed reagents/materials/analysis tools: XXY XHQ ZXQ

Wrote the paper: TYZ LC

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Abbreviations

BMI

body Mass Index

CVD

cardiovascular disease

DBP

diastolic blood pressure

FRS

Framingham 10-year general cardiovascular disease risk score

HDL-C

high density lipoprotein cholesterol

LDL-C

low density lipoprotein cholesterol

SBP

systolic blood pressure

TC

serum total cholesterol

T2DM

type 2 diabetes mellitus

References

1. Hu H, Sawhney M, Shi L, Duan S. A systematic review of the direct economic burden of type 2 diabetes in China. *Diabetes Ther.* 2015;6(1):7–16. <https://doi.org/10.1007/s13300-015-0096-0>.
2. World Health Organization. Global report on diabetes. Geneva: World Health Organization. https://www.who.int/substance_abuse/publications/global_alcohol_report/en/. Accessed 8 Aug 2018.
3. Prendergast C, Gidding SS. Cardiovascular risk in children and adolescents with type 2 diabetes mellitus. *Curr Diab Rep.* 2014;14(2):454.
4. Bhupathiraju SN, Hu FB. Epidemiology of Obesity and Diabetes and Their Cardiovascular Complications. *Circ Res.* 2016;118(11):1723-1735.
5. Tanaka S, Horimai C, Katsukawa F. Ethnic differences in abdominal visceral fat accumulation between Japanese, African-Americans, and Caucasians: a meta-analysis. *Acta Diabetol* 2003;40 Suppl 1:S302-4
6. Reaven GM. Insulin resistance: the link between obesity and cardiovascular disease. *Med Clin North Am.* 2011;95(5):875-892.
7. Carroll C, Naylor E, Marsden P, et al. How do people with Type 2 diabetes perceive and respond to cardiovascular risk? [J]. *Diabet Med.* 2003, 20(5): 355-360.
8. Wang T, Xu Y, Xu M, et al. Awareness, treatment and control of cardiometabolic disorders in Chinese adults with diabetes: a national representative population study [J]. *Cardiovasc Diabetol.* 2015, 14: 28.
9. Tabet, F, Remaley, A. T, Segaliny, A. I., The 5A Apolipoprotein A-I Mimetic Peptide Displays Antiinflammatory and Antioxidant Properties In Vivo and In Vitro [J]. *Arteriosclerosis Thrombosis & Vascular Biology*, 30(2):246-252.
10. Krimbou L, March M, Genest J. New insights into the biogenesis of human high-density lipoproteins. *Curr Opin Lipidol*, 2006, 17:258-267.
11. Tanigawa H, Billheimer JT, Tohyama J, et al. Expression of cholesteryl ester transfer protein in mice promotes macrophage reverse cholesterol transport. *Circulation*, 2007, 116:1267-1273.

12. Vaisar T, Pennathur S, Green PS, et al. Shotgun proteomics implicates protease inhibition and complement activation in the antiinflammatory properties of HDL. *J Clin Invest*, 2001;117:746-756.
13. Ansell BJ, Fonarow GC, Fogelman AM. The paradox of dysfunctional high-density lipoprotein. *Curr Opin Lipidol*, 2007, 18:427-134.
14. Krause BR, Remaley AT. Reconstituted HDL for the acute treatment of acute coronary syndrome[J]. *Curr Opin Lipidol*. 2013 Dec;24(6):480-6.
15. Yoshida M, Mita T, Yamamoto R, Shimizu T, Ikeda F, Ohmura C, et al. Combination of the Framingham risk score and carotid intima-media thickness improves the prediction of cardiovascular events in patients with type 2 diabetes. *Diabetes Care* 2012;35:178-80.
16. D'Agostino RB, Sr., Vasan RS, Pencina MJ, Wolf PA, Cobain M, Massaro JM, et al. General cardiovascular risk profile for use in primary care: the Framingham Heart Study. *Circulation* 2008;117:743-53.
17. Hafiane A(1), Kellett S, Genest J. Treatment options for low high-density lipoproteins. *Curr Opin Endocrinol Diabetes Obes*[J]. 2014 Apr;21(2):134-9.
18. Joy TR(1). Novel HDL-based therapeutic agents[J]. *Pharmacol Ther*. 2012 Jul;135(1):18-30.
19. Wannamethee SG, Shaper AG, Lennon L, Morris RW. Metabolic syndrome vs Framingham Risk Score for prediction of coronary heart disease, stroke, and type 2 diabetes mellitus. *Arch Intern Med* 2005;165:2644-50.
20. Stern MP, Williams K, Gonzalez-Villalpando C, Hunt KJ, Haffner SM. Does the metabolic syndrome improve identification of individuals at risk of type 2 diabetes and/or cardiovascular disease? *Diabetes Care* 2004;27:2676-81.
21. Krisela Steyn, Albertino Damasceno. Lifestyle and Related Risk Factors for Chronic Diseases[M]. PubMed, 2006.
22. Dhevaksha Naidoo, Adrian Schembri, Marc Cohen. The health impact of residential retreats: A systematic review[J]. *Bmc Complementary & Alternative Medicine*, 2018, 18(1).
23. E W Almquist, R R Brinkman, S Wiggins, et al. Psychological consequences and predictors of adverse events in the first 5 years after predictive testing for Huntington's disease[J]. *Clinical Genetics*, 2003, 64(4):300-309.
24. Samuel D Gosling, Peter J Rentfrow, William B Swann. A Very Brief Measure of the Big-Five Personality Domains[J]. *Journal of Research in Personality*, 2003, 37(6):504-528.
25. Bacha F, Gungor N, Lee S, Arslanian SA. In vivo insulin sensitivity and secretion in obese youth: what are the differences between normal glucose tolerance, impaired glucose tolerance, and type 2 diabetes? *Diabetes Care*. 2009;32(1):100-105.
26. Burns SF, Lee S, Bacha F, Tfayli H, Hannon TS, Arslanian SA. Pre-diabetes in overweight youth and early atherogenic risk. *Metabolism*. 2014;63(12):1528-1535.
27. Zhang XF, Attia J, D'Este K, Yu XH, Wu XG. Prevalence and magnitude of classical risk factors for coronary heart disease in a cohort of 4400 Chinese steelworkers over 13.5 years follow-up. *Eur J Cardiovasc Prev Rehabil* 2004, 11(2):113-120.
28. Simpson S H, Johnson J A, Biggs R S, et al. Greater effect of enhanced pharmacist care on cholesterol

- management in patients with diabetes mellitus: a planned subgroup analysis of the Study of Cardiovascular Risk Intervention by Pharmacists (SCRIP).[J]. 2012, 24(3):389-394.
- 29.Wu Z, Yao C, Zhao D, Wu G, Wang W, Liu J, Zeng Z, Wu Y: Sino-MONICA project: a collaborative study on trends and determinants in cardiovascular diseases in China, Part i: morbidity and mortality monitoring. *Circulation* 2001, 103(3):462-468.
- 30.Marialaura Bonaccio, Augusto Di Castelnuovo, Simona Costanzo, et al. Chili Pepper Consumption and Mortality in Italian Adults. *J Am Coll Cardiol*. 2019; 74(25). doi:10.1016/j.jacc.2019.09.068.31
- 31.Jun Lv, Lu Qi, Canqing Yu, et al. Consumption of spicy foods and total and cause specific mortality: population based cohort study. *BMJ*. 2015; 351: h3942.
- 32.Mustafa C , Benjamin L , Oreste G . The Association of Hot Red Chili Pepper Consumption and Mortality: A Large Population-Based Cohort Study[J]. *PLOS ONE*, 2017, 12(1):e0169876-.
- 33.Yang D , Luo Z , Ma S , et al. Activation of TRPV1 by Dietary Capsaicin Improves Endothelium-Dependent Vasorelaxation and Prevents Hypertension[J]. *Cell Metabolism*, 2010, 12(2):0-141.
- 34.Emons W H, Meijer R R, Denollet J. Negative affectivity and social inhibition in cardiovascular disease: evaluating type-D personality and its assessment using item response theory.[J]. 2007, 63(1):27-39.
35. Sturmer, T. Personality, lifestyle, and risk of cardiovascular disease and cancer: follow-up of population based cohort[J]. *BMJ*, 332(7554):1359-0.
36. Aysha Almas, Jette Moller, Romaina Iqbal. Effect of neuroticism on risk of cardiovascular disease in depressed persons-a Swedish population-based cohort study[J]. *Bmc Cardiovascular Disorders*, 2017, 17(1):185.