Computers in Biology and Medicine 53 (2014) 105–114

Contents lists available at ScienceDirect

Computers in Biology and Medicine

journal homepage: www.elsevier.com/locate/cbm

Exploring the effects of intervention for those at high risk of developing type 2 diabetes using a computer simulation☆,☆☆

Senlin Luo [a], Songjing Chen [a,*], Limin Pan [a], Tiemei Zhang [b], Longfei Han [a], Yue Wang [a], Qamas Gul Khan Safi [a]

[a] School of Information and Electronics, Beijing Institute of Technology, 100081 Beijing, China
[b] Department of Cell Biology, The Key Laboratory of Geriatrics, Beijing Institute of Geriatrics, Ministry of Health, 100730 Beijing, China

ARTICLE INFO

Article history:
Received 18 November 2013
Accepted 31 May 2014

Keywords:
High risk
Intervention
Simulated computation
Type 2 diabetes
Transition

ABSTRACT

A simulation based computational method was conducted to reflect the effect of intervention for those at high risk of type 2 diabetes. Hierarchy Support Vector Machines (H-SVMs) were used to classify high risk. The proportion transitioning from the high risk state to moderate state, low state or the normal state was calculated. When Body Mass Index (BMI) decreased by 5% (weight loss 3–5 kg), the proportion of Class A transferring to a lower state was 15–25%, and risk also appeared reduced for Class B1. In Class C, when cholesterol (CHOL) was decreased by 2.5% (0.13–0.34 mmol/L), 10–25% transitioned to a lower risk state. The method could help determine risk transition by the adjustment of sensitive risk factors. This might provide the basis for implementing intervention in cases in a high risk state.

1. Introduction

Type 2 diabetes is a serious and expensive disease. Lifestyle intervention is effective and cost-effective from the perspective of the health system and society [1]. It is widely recognized that the incidence of type 2 diabetes is high and increasing gradually throughout the world. In order to predict the effect of intervention at the initial stage, simulated computational research was conducted. This research could provide effective guidance and improve the efficiency of intervention. Recent research demonstrates that the risk of type 2 diabetes can be reduced by successful lifestyle intervention [2–4]. Interventions such as weight loss and enhanced physical activity are significant predictors of risk reduction [5,6].

Lifestyle modification focused on modest weight loss (5–10%) and moderately intense physical activity could significantly reduce the incidence of type 2 diabetes (by 58%, as shown in the Diabetes Prevention Program (DPP)) and cardiometabolic risk factors in high-risk individuals [7,8]. The World Health Organization (WHO) strongly recommends strategies for the prevention of type 2 diabetes, which has a strong association with obesity [10]. Several intervention studies, in China ("Da-Qing Study") [11,12], in Europe ("Malmo study" [13,14], "Finnish Diabetes Prevention Study" [15–17]) and in the United States ("Diabetes Prevention Program") [18] have shown that lifestyle changes were able to reduce the incidence of type 2 diabetes by around 50% among at-risk individuals. Rautio [19] assessed the predictors of success with lifestyle intervention (weight loss $\geq 5\%$ and improved glucose tolerance) in individuals at high risk in a 1-year follow-up in a primary health care setting. The intervention period required a long time, usually six months to one year, or even much longer, until the study period was finished, before the effect of the intervention could be known.

The aim of this study was to simulate the effect of intervention in those at high risk of type 2 diabetes. According to their present health status, sensitive risk factors were adjusted, and the effect of intervention was simulated. At the same time, the importance of the sensitive risk factors was verified. This research could supply predictions of the effect of intervention in the early stages of intervention implementation. That might help to give effective guidance, improve the efficiency of the intervention, and save money.

2. Materials and methods

2.1. Materials

The research was undertaken on 59,839 cross-sectional health examination records in the Chinese Academy of Sciences, Mining

☆The foreign doctor student (an English linguist) did some contribution on the English polishing work. So we add him as an author. And Haixiu Zhao did less work for this article and graduated for school. So we removed her from the author list.

☆☆This is a special focus paper published in connection with the 2nd International Conference on Biomedical Engineering and Biotechnology (iCBEB 2013), held in Wuhan, China, October 11-13, 2013.

* Corresponding author.
E-mail address: 3120100321@bit.edu.cn (S. Chen).

http://dx.doi.org/10.1016/j.compbiomed.2014.05.015
0010-4825/

Bureau and Public Security Bureau in Beijing, Xi'an, Wuxi and Anyang in China from 2001 to 2008. The 59,839 cases included 34,377 men (57.40%) and 25,462 women (42.60%), all adults aged 20–84 years without diabetes. The outcome without diabetes was diagnosed on the basis of the 1997 criteria [20]. The specific distribution of subjects judged by gender and age is presented in Table 1. The validation data came from the Beijing Hospital Medical Center, including 1132 high risk subjects in 2007 and 2008, consisting of 59% men and 41% women. The validation data were independent of the experimental data.

The high risk state was identified using the risk state determination (RSD) system which was available at http://www.isclab.org/rsd/RSDAssess.php. The high risk criteria are shown in Table 2. A schematic diagram of the RSD system is shown in Fig. 1. In the RSD system, the inputs were risk factors such as Body Mass Index (BMI), Cholesterol (CHOL), Triglyceride (TG), Diastolic Blood Pressure (DBP), High Density Lipoprotein (HDL), age, etc., and the output was the risk state. The 6-year follow-up test result of the RSD system is given in Table 3. Four risk states were determined using RSD, including high risk, moderate risk, low risk and the normal state, as shown in Tables 4 and 5.

Table 1
Subject distribution by gender and age.

Age	Men		Women		Total number
	Number of samples	Percentage	Number of samples	Percentage	
20–24	1465	61.30	924	38.70	2389
25–29	4213	65.70	2195	34.30	6408
30–34	3564	62.40	2151	37.60	5715
35–39	4386	60.30	2886	39.70	7272
40–44	3925	56.70	2994	43.30	6919
45–49	3228	53.60	2789	46.40	6017
50–54	3090	50.50	3034	49.50	6124
55–59	2542	49.60	2581	50.40	5123
60–64	2797	56.50	2151	43.50	4948
65–69	2251	58.20	1617	41.80	3868
70–74	1652	59.50	1126	40.50	2778
75–79	880	56.00	692	44.00	1572
80–84	384	54.40	322	45.60	706
Total	34,377	57.40	25,462	42.60	59,839

The distribution of high risk subjects by gender and age is shown in Table 6.

2.2. Methods

The high risk state, the moderate risk state, the low risk state and the normal state are the four risk states of type 2 diabetes. Those in the high risk state have the highest risk of developing type 2 diabetes among these four states. Based on high risk cross-sectional data, a simulated computational method was proposed in this research. Qualitative analysis and quantitative calculation were combined to realize the high risk simulated computational model, and machine learning and mathematical statistics methods were applied to construct this model. Constructing subgroup attribution models by H-SVMs, sensitive risk factors were quantitatively adjusted in the corresponding subgroup. The high risk state was distributed into four subgroups: Class A; Class B1; Class B2 and Class C. Then we computed the transition state proportions from high risk to lower states (moderate risk, low risk and normal) separately. There were four main steps in the entire process: subgroup attribution; degree of intervention computation; RSD determination and statistical analysis.

2.2.1. Subgroup attribution

In order to further refine the high risk state, three grades were divided through subgroup attribution. These were the high degree (Class A), moderate degree (Classes B1 and B2) and low degree (Class C). The process of generating the classification model is shown in Fig. 2.

2.2.1.1. Sensitive risk factor determination. According to the sensitivity calculation results [21], the sensitive risk factors for high risk subjects were determined. Sensitive risk factors have much more influence on changes in glucose than other factors and are presented in Table 7. The four subgroups had different sensitive risk factors and different high risk grades. Class A had the highest risk in the high risk state, followed by Classes B1, B2 and C.

2.2.1.2. H-SVMs classification model training. The classification model was trained using the H-SVMs algorithm. At first, men > 50 at high risk were divided into four classes: Class A, Class B1, Class B2 and Class C, as shown in Fig. 3. Class A was separated from

Table 2
The high risk criteria.

No.	High risk criteria
1	GLU > 5.85 mmol/L (except 5.85 < GLU < 6.00 mmol/L, age ≥ 60, BMI < 26 kg/m^2 and without family history of diabetes)
2	BMI > 26.80 kg/m^2, CHOL > 5.18 mmol/L and TG > 1.70 mmol/L (all three points must be satisfied)
3	GLU > 5.60 mmol/L, DBP > 85 mmHg, TG > 1.70 mmol/L or HDL < 1.03 mmol/L (men), HDL < 1.29 mmol/L (women) (two of the four points must be satisfied)
4	Waist > 90 cm (men), Waist > 80 cm (women), TG > 1.70 mmol/L and CHOL > 5.18 mmol/L (all three points must be satisfied)

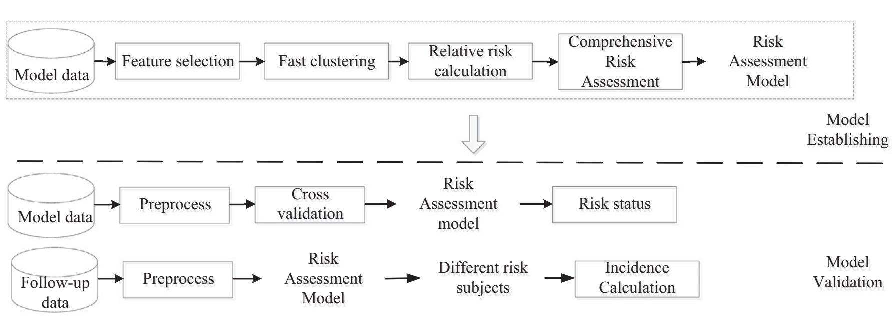

Fig. 1. The schematic diagram of RSD system.