# Impact of healthy lifestyle on the risk of type 2 diabetes mellitus in southwest China: A prospective cohort study

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### **Keywords**

Healthy lifestyle, Incidence, Type 2 diabetes mellitus

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J Diabetes Investig 2022; 13: 2091–2100

doi: 10.1111/jdi.13909

## ABSTRACT

**Aims:** To explore the influence of nine healthy lifestyle factors on the risk of type 2 diabetes mellitus in adults in Guizhou, China.

**Methods:** Data were obtained from a large population-based prospective cohort study in Guizhou Province, China. A total of 7,319 participants aged ≥18 years without diabetes at baseline were included in this study and were followed up from 2016 to 2020. A healthy lifestyle score was calculated based on the number of healthy lifestyle factors. **Results:** During an average of 7.1 person-years of follow-up, 764 participants were diagnosed with type 2 diabetes mellitus. Compared with those of participants who scored 0–3 for a healthy lifestyle, the hazard ratios (95% confidence intervals) of those who scored 4, 5, 6, and ≥7 were 0.676 (0.523–0.874), 0.599 (0.464–0.773), 0.512 (0.390–0.673), and 0.393 (0.282–0.550), respectively, showing a gradual downward trend (*P* for trend <0.01). More importantly, they had lower fasting and 2 h post-load plasma glucose levels and fewer changes in plasma glucose levels during follow-up. If ≥7 healthy lifestyle factors were maintained, 33.8% of incident diabetes cases could have been prevented. Never smoking was the strongest protective factor against type 2 diabetes mellitus. **Conclusions:** A healthy lifestyle can effectively decrease plasma glucose levels and

reduce the incidence of type 2 diabetes mellitus in adults in Guizhou, China. In addition, not smoking may be an effective way to prevent type 2 diabetes mellitus.

# INTRODUCTION

Diabetes is one of the fastest-growing diseases worldwide and poses a serious challenge to global public health<sup>1,2</sup>, with approximately 537 million adults (20–79 years) with diabetes in 2021 worldwide<sup>3</sup>. The largest number of patients with diabetes live in China, causing a heavy burden of the disease on the country. With economic development, lifestyle changes, and the acceleration of population aging, the prevalence of diabetes is continuously increasing in China. The latest research showed that its prevalence in adults in China was 11.2%, according to the World Health Organization<sup>4</sup>.

Studies have shown that a healthy lifestyle may reduce the risk of type 2 diabetes mellitus<sup>5,6</sup>. A large prospective cohort study observed that a healthy lifestyle increased life expectancy free of diabetes by 10.3 years for men and 12.3 years for

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women<sup>7</sup>. A cohort study in the United Kingdom showed that the risk of diabetes in men was reduced by half owing to a healthy lifestyle<sup>8</sup>. Another cohort study demonstrated that a healthy lifestyle might contribute to diabetes prevention among African Americans<sup>9</sup>. A prospective cohort study in China found that the combination of the amount of physical activity, diet, body mass index (BMI), and waist-to-hip ratio accounted for 72.6% of the etiology of diabetes<sup>10</sup>. Another study also established that lifestyle factors were associated with an increased diabetes burden in China<sup>11</sup>. The benefits of a healthy lifestyle on glucose metabolism have also been demonstrated in pregnant women<sup>12,13</sup>. Several randomized controlled trials have shown that the onset of type 2 diabetes mellitus can be delayed or prevented via lifestyle intervention among people with impaired glucose regulation, or even normal glucose tolerance can be restored<sup>14-16</sup>.

However, most previous studies only focused on diet, physical activity, smoking, alcohol intake, and a few other factors.

Received 6 May 2022; revised 18 August 2022; accepted 5 September 2022

Furthermore, little is known about the effects of lifestyle on glucose metabolism in ethnic minority regions in China. Therefore, this study aimed to identify the influence of nine lifestyle factors, such as smoking; alcohol intake; sedentary behavior; sleep time; BMI; and the intake of vegetables, fruits, edible oils, and salt, on the risk of type 2 diabetes mellitus in adults in Guizhou Province, which has the lowest prevalence of diabetes in China<sup>4</sup>. Furthermore, we assessed the contribution of healthy lifestyle factors to the incidence of diabetes and the importance of each constituent factor.

# **METHODS**

#### Study population

The data were obtained from the Guizhou Population Health Cohort Study (GPHCS), a large population database that aimed to investigate the epidemic of chronic diseases and risk factors. Details regarding the GPHCS cohort have been published previously<sup>17</sup>. The baseline survey covered 12 districts in Guizhou Province using multistage proportional stratified cluster sampling from 2010 to 2012. We included a total of 9,280 permanent residents aged  $\geq 18$  years in the study. The participants were followed up from 2016 to 2020. Of these, 8,163 participants completed the follow-up (87.96%). In this study, we excluded those who had been diagnosed with diabetes (n = 809) or had missing diabetes data (n = 34) at baseline, were lost to follow-up (n = 994), had died during the followup period (n = 106), and had missing diabetes data at followup (n = 18). Finally, the remaining 7,319 participants were included in the analysis. The flow chart of the study is shown in Figure 1. The study was approved by the Institutional Review Board of the Guizhou Center for Disease Control and Prevention (no. S2017-02). In addition, written informed consent was obtained from all participants.

### Assessment of lifestyle behaviors and other covariates

Information on smoking, alcohol consumption, educational background, sedentary behavior, sleep status, history of diseases, and family history of diabetes was collected from the self-reported data of each participant. The food frequency question-naire was used to assess the frequency and quantity of various foods consumed in the past 12 months. The intake of edible oil and salt in a family in the past 30 days was assessed using a family questionnaire and then converted into daily intake for each participant according to the number of people in a family.

After at least 10 h of overnight fasting, a 75 g oral glucose tolerance test was conducted for each participant. A venous blood sample was collected before and 2 h after glucose administration. Plasma glucose was detected using the hexokinase method within 4 h. After centrifugation, serum separated from the remaining blood samples was stored at  $-20^{\circ}$ C and transferred to Guizhou Center for Disease Control and Prevention to detect levels of triglycerides, total cholesterol, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol (Olympus 400 Analyzer; Beckman Coulter, Brea, CA, USA).

Body height, weight, and blood pressure were measured by strictly and uniformly trained staff. BMI was calculated by dividing the weight by height squared  $(kg/m^2)$ .

According to the recommendations of Chinese dietary guidelines<sup>18</sup> and previous studies<sup>19–22</sup>, healthy lifestyle factors include never smoking, never drinking, sedentary time <6 h/day, sleeping time 7–9 h/day, having a BMI between 18.5 and 23.9 kg/ m<sup>2</sup>, vegetable intake  $\geq$ 300 g/day, fruit intake  $\geq$ 200 g/day, edible oil intake  $\leq$ 30 g/day, and salt intake  $\leq$ 6 g/day. A healthy lifestyle score was constructed based on these nine lifestyle factors. For each healthy lifestyle, participants who met the standard were assigned 1 point. Higher scores indicated healthier lifestyles than those with lower scores. Due to the small score range, participants with a score of  $\leq$ 3 were combined into one group, and those with a score of  $\geq$ 7 were combined into another group.

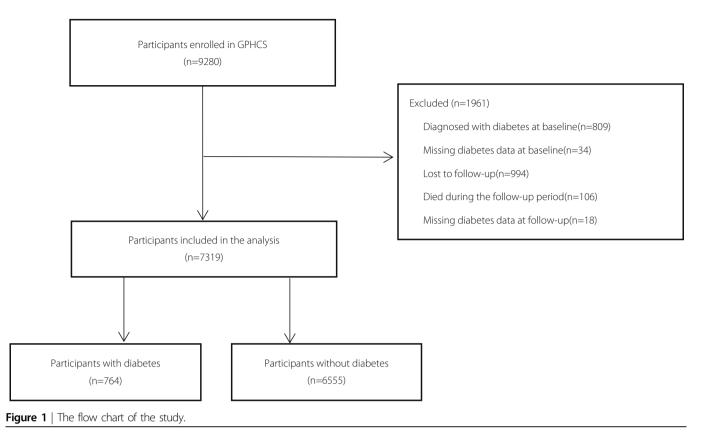
Diabetes was defined as a fasting plasma glucose concentration of  $\geq$ 7.0 mmol/L, 2 h glucose concentration of  $\geq$ 11.1 mmol/L, or having been diagnosed with diabetes by township or community and above hospitals. According to the 1999 World Health Organization criteria, impaired glucose tolerance is defined as a fasting plasma glucose concentration of <7.0 mmol/L and a 2 h glucose concentration of 7.8– 11.0 mmol/L; impaired fasting glucose is defined as a fasting plasma glucose concentration of 6.1–6.9 mmol/L and 2 h glucose concentration of <7.8 mmol/L<sup>23,24</sup>. Lastly, hypertension included those with a systolic blood pressure  $\geq$ 140 mmHg and/ or diastolic blood pressure  $\geq$ 90 mmHg, or self-reported hypertension<sup>25</sup>.

### Statistical analysis

The Statistical Package for the Social Sciences (version 23.0; IBM Corporation, Armonk, NY, USA) and R (version 4.1.2; Lucent Technologies Inc., Murray Hill, NJ, USA) were used to perform statistical analyses. Person-years were used as the time variable. The person-years were calculated from the baseline survey to the onset of diabetes or the end of follow-up, and the incidence density of different healthy lifestyle groups was calculated. A Cox proportional hazards regression model was used to evaluate the risk of type 2 diabetes mellitus. The hazard ratio and 95% confidence interval (CI) were calculated with a healthy lifestyle score of 0–3 as reference.

The population attributable risk percentage (PAR%) was calculated to evaluate the effect of an increasing number of healthy lifestyle factors on the incidence of type 2 diabetes mellitus under the assumption of causality. Considering the distribution of the number of healthy lifestyle factors in our study population, PAR% and 95% CI for participants maintaining  $\geq$ 4,  $\geq$ 5,  $\geq$ 6, and  $\geq$ 7 healthy lifestyle factors were estimated respectively.

In addition, we subtracted one of the nine healthy lifestyle factors at a time and calculated the hazard ratio and 95% CI for incident type 2 diabetes mellitus to assess the importance of each healthy lifestyle factor.



Several sensitivity analyses were conducted: (i) participants who had been diagnosed with diabetes for more than 5 years at follow-up were excluded; (ii) participants with prediabetes at follow-up were excluded; (iii) participants with hypertension at baseline were excluded; (vi) the cutoff value of sedentary time from 6 to 8 h/day was adjusted; (v) ethnicity was adjusted as a confounding factor. A two-sided *P*-value <0.05 was considered statistically significant.

# RESULTS

### Baseline characteristics of participants

A total of 7,319 participants with an average age of  $43.7 \pm 14.9$  years were included in this study. The average follow-up was  $7.1 \pm 1.3$  person-years. During the follow-up period, 764 participants were diagnosed with type 2 diabetes mellitus. According to whether diabetes occurs at follow-up and considering healthy lifestyle scores, the baseline characteristics of participants are shown in Tables 1 and 2, respectively. Among those diagnosed with diabetes during the follow-up period, the proportion of young people; urban population; and participants with appropriate sleep time, never smoking, having optimal BMI, meeting the intake standards of fruit, edible oil, and salt was lower, while the proportion of participants with a low education level accompanied with dyslipidemia and hypertension was higher (P < 0.05 or 0.01). There was no significant

difference in the proportion of participants with sedentary time <6 h/day, high vegetable intake, never drinking, and a family history of diabetes, regardless of whether diabetes occurred (P > 0.05). With the increase in healthy lifestyle scores, the proportion of men, urban population, combined dyslipidemia, and hypertension decreased, and the proportion of young people, participants with a low education level, sedentary time <6 h/day, appropriate sleep time, optimal BMI, never smoking, never drinking, and meeting the intake standards of vegetable, fruit, edible oil, and salt gradually increased (all P < 0.01).

# The influence of each healthy lifestyle factor on the risk of type 2 diabetes mellitus

The influence of each healthy lifestyle factor on the risk of type 2 diabetes mellitus is shown in Figure 2. Never smoking, never drinking, appropriate sleep time, optimal BMI, low intake of edible oil and salt, and high fruit intake were protective factors against type 2 diabetes mellitus. Subgroup analysis showed that optimal BMI and low intake of edible oil and salt were protective factors for men; appropriate sleep time, optimal BMI, low intake of edible oil and salt, and high fruit intake were protective factors for women; and optimal BMI, low salt intake, and high fruit intake were protective effect of a healthy lifestyle was consistent between the total participants and rural participants.

Characteristic	Total ( $n = 7,319$ )	Diabetes ( $n = 764$ )	Non-diabetes ( $n = 6,555$ )	P value
Men	3427 (46.8)	371 (48.6)	3056 (46.6)	0.309
Age <45 years	4043 (55.2)	339 (44.4)	3704 (56.5)	< 0.01
Urban	2496 (34.1)	225 (29.5)	2271 (34.6)	0.004
Education years <9 years	4164 (56.9)	494 (64.7)	3670 (56.0)	< 0.01
Sedentary behavior <6 h/day	5922 (80.9)	627 (82.1)	5295 (80.8)	0.391
Sleep time 7–9 h/day	5723 (78.2)	565 (74.0)	5158 (78.7)	0.003
Never smoking	5240 (71.6)	522 (68.3)	4718 (72.0)	0.034
Never drinking	5002 (68.3)	508 (66.5)	4494 (68.6)	0.245
18.5 <u>≤</u> BMI <u>≤</u> 23.9 kg/m <sup>2</sup>	4668 (63.8)	428 (56.0)	4240 (64.7)	< 0.01
Vegetable intake ≥300 g/day	4949 (67.6)	538 (70.4)	4411 (67.3)	0.080
Fruit intake ≥200 g/day	424 (5.8)	27 (3.5)	397 (6.1)	0.005
Edible oil intake ≤30 g/day	2542 (34.7)	226 (29.6)	2316 (35.3)	0.002
Salt intake ≤6 g/day	2110 (28.8)	182 (23.8)	1928 (29.4)	0.001
Dyslipidemia	4103 (56.1)	464 (60.7)	3639 (55.5)	0.006
Hypertension	1756 (24)	223 (29.2)	1533 (23.4)	< 0.01
Family history of diabetes	98 (1.8)	11 (2.0)	87 (1.8)	0.754

Table 1 | Baseline characteristics of participants according to whether diabetes occurs at follow-up. Values are numbers (percentages)

The information on family history of diabetes was missing in 1925 participants. BMI, body mass index.

Table 2	Baseline characteristics of	participants acco	ording to the health	y lifestyle scores.	Values are numbers	(percentages)
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Characteristic	Healthy lifestyle score					
	0–3 ( <i>n</i> = 1,087)	4 ( <i>n</i> = 1,534)	5 (n = 1,874)	6 ( <i>n</i> = 1,780)	7– ( <i>n</i> = 1,044)	
Men	853 (78.47)	880 (57.37)	813 (43.38)	584 (32.81)	297 (28.45)	<0.01
Age <45 years	531 (48.85)	772 (50.33)	1004 (53.58)	1060 (59.55)	676 (64.75)	< 0.01
Urban	458 (42.13)	570 (37.16)	642 (34.26)	520 (29.21)	306 (29.31)	< 0.01
Education years <9 years	511 (47.01)	851 (55.48)	1107 (59.07)	1082 (60.79)	613 (58.72)	< 0.01
Sedentary behavior <6 h/day	811 (74.61)	1313 (85.59)	1699 (90.66)	1672 (93.93)	1009 (96.65)	< 0.01
Sleep time 7–9 h/day	565 (51.98)	1078 (70.27)	1514 (80.79)	1579 (88.71)	987 (94.54)	< 0.01
Never smoking	256 (23.55)	811 (52.87)	1360 (72.57)	1562 (87.75)	1013 (97.03)	< 0.01
Never drinking	307 (28.24)	875 (57.04)	1460 (77.91)	1595 (89.61)	1003 (96.07)	< 0.01
18.5 ≤BMI ≤23.9 kg/m²	431 (39.83)	815 (53.3)	1121 (59.88)	1390 (78.18)	911 (87.26)	< 0.01
Vegetable intake ≥300 g/day	457 (42.24)	868 (56.66)	1282 (68.81)	1418 (80.98)	924 (91.21)	< 0.01
Fruit intake ≥200 g/day	25 (2.32)	42 (2.77)	90 (4.84)	124 (7.07)	143 (13.94)	< 0.01
Edible oil intake ≤30 g/day	108 (9.94)	265 (17.28)	583 (31.11)	785 (44.1)	801 (76.72)	< 0.01
Salt intake ≤6 g/day	86 (7.92)	223 (14.54)	402 (21.45)	626 (35.17)	773 (74.04)	< 0.01
Dyslipidemia	700 (64.4)	916 (59.71)	1051 (56.08)	921 (51.74)	515 (49.33)	< 0.01
Hypertension	320 (29.44)	440 (28.68)	455 (24.28)	364 (20.45)	177 (16.95)	< 0.01
Family history of diabetes	21 (2.49)	19 (1.72)	24 (1.74)	17 (1.31)	17 (2.21)	0.317

The information on family history of diabetes was missing in 1925 participants. BMI, body mass index.

### Effect of healthy lifestyle score on type 2 diabetes mellitus

The results of Cox proportional hazards regression are presented in Table 3. In this study, the incidence of type 2 diabetes mellitus was 14.7/1,000 person-years. With the increasing number of healthy lifestyle factors, the incidence of diabetes gradually decreased. Compared with those of participants who scored 0–3 for a healthy lifestyle, the hazard ratios of those who scored 4, 5, 6, and  $\geq$ 7 were 0.676 (95% CI: 0.523–0.874), 0.599 (95% CI: 0.464–0.773), 0.512 (95% CI: 0.390–0.673), and 0.393 (95% CI: 0.282–0.550), respectively, showing a gradual downward trend (*P* for trend <0.01). Compared with that in participants with a score of only 0–3 healthy lifestyle factors, the risk of developing diabetes in participants with a score of  $\geq$ 7 healthy lifestyle factors decreased by 60.7%. The PAR% of the incidence of type 2 diabetes mellitus was 10.5% (95% CI: 5.7–15.0%) if all participants maintained  $\geq$ 4 healthy lifestyle factors. When the number of healthy lifestyle factors was increased to  $\geq$ 5,  $\geq$ 6, or  $\geq$ 7, the PAR% was 15.9% (95% CI: 8.8–22.5%), 23.3% (95% CI: 12.5–32.7%), and 33.8% (95% CI: 15.1–48.4%), respectively. Subgroup analysis showed that higher healthy

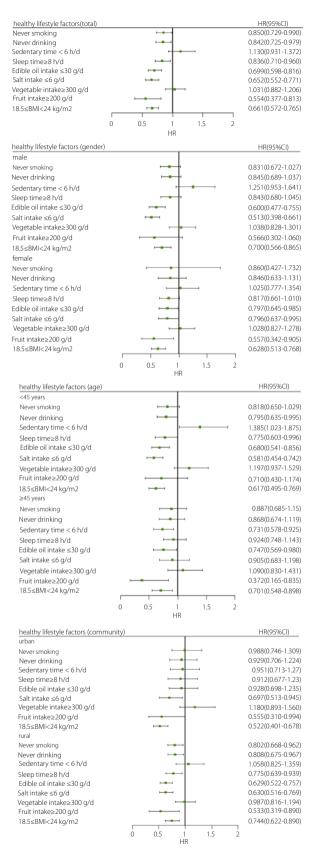


Figure 2 | The influence of each healthy lifestyle factor on the risk of type 2 diabetes mellitus.

lifestyle scores indicated a lower risk of type 2 diabetes mellitus regardless of sex, age, and community. Furthermore, the nine healthy lifestyle factors included in this study appeared to be more effective in preventing type 2 diabetes mellitus in men than in women (Figure 3). To assess the importance of each healthy lifestyle factor, the hazard ratio and 95% CI for incident type 2 diabetes mellitus were calculated after subtracting one of the nine healthy lifestyle factors at a time. The results showed that the hazard ratio changed with each factor subtracted; never smoking was the strongest protective factor against type 2 diabetes mellitus (Figure 4).

### Effect of healthy lifestyle score on plasma glucose levels

The association between healthy lifestyle scores and changes in plasma glucose levels from baseline to follow-up is presented in Table 4. No differences in fasting plasma glucose and 2 h post-load plasma glucose were observed in each group at baseline. Participants with a healthy lifestyle score of  $\geq$ 4 had lower fasting and 2 h post-load plasma glucose levels and fewer changes in plasma glucose levels during follow-up than participants with a healthy lifestyle score of 0–3.

### Sensitivity analysis

In this study, sensitivity analysis showed that the results obtained with each method were consistent with the main analysis results (Table S1).

### DISCUSSION

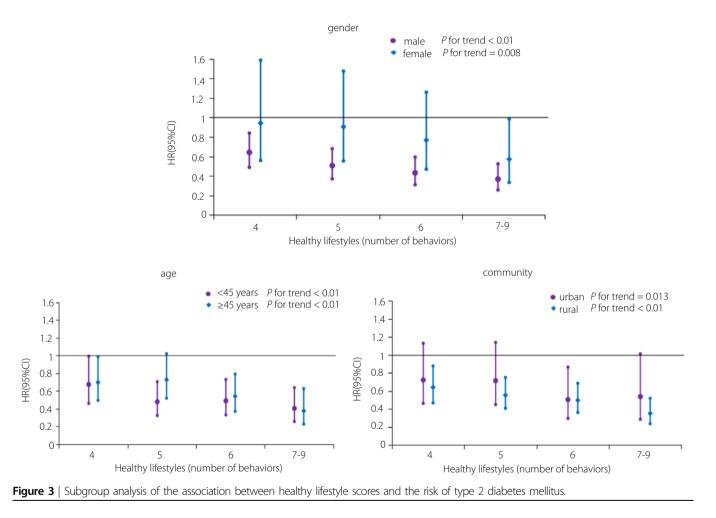
In this study, we comprehensively explored the influence of nine lifestyle factors on the risk of type 2 diabetes mellitus in adults in Guizhou, China. From the results, we observed that never smoking, never drinking, appropriate sleep time, optimal BMI, low intake of edible oil and salt, and high fruit intake were protective factors against type 2 diabetes mellitus. With the increase in the number of healthy lifestyle factors, the risk of type 2 diabetes mellitus gradually decreased, especially among men. Compared with those in participants with a healthy lifestyle score of only 0-3, the plasma glucose levels in participants with a score of  $\geq 4$  were lower at follow-up, and the risk of developing diabetes in participants with a score of  $\geq$ 7 decreased by 60.7%. If  $\geq$ 7 healthy lifestyle factors were maintained, 33.8% of incident diabetes cases could have been prevented. The strongest protective factor against diabetes was never smoking.

Our results confirm that a healthy lifestyle can reduce the risk of type 2 diabetes mellitus, which is consistent with previous studies<sup>6–10,26</sup>. A large prospective cohort study examined the effects of five lifestyle factors (smoking, alcohol intake, BMI, physical activity, and diet) on the risk of type 2 diabetes mellitus. The results showed that participants with more healthy lifestyle factors had a lower risk of type 2 diabetes mellitus<sup>7</sup>. A 10 year cohort study showed that increased lifestyle scores, especially dietary fiber intake, were associated with a lower risk of diabetes<sup>27</sup>. Li et al.<sup>6</sup> analyzed two independent cohort studies

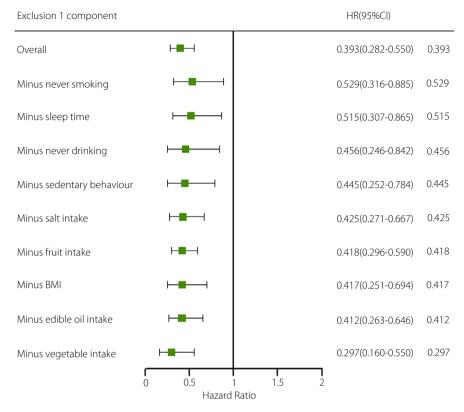
Healthy lifestyle score	Cases	Person-years of follow-up	Incident density (/1,000 PYs)	Hazard ratio (95% CI)	P value
	Cases	reison years or tonow up			
Total	764	51,924.01	14.71	NA	NA
0–3	154	7,491.4	20.56	1.000 (ref)	NA
4	181	10,684.93	16.94	0.676 (0.523–0.874)	0.003
5	183	13,247.53	13.81	0.599 (0.464–0.773)	< 0.01
6	160	12,805.24	12.49	0.512 (0.390-0.673)	< 0.01
7—	86	7,694.91	11.18	0.393 (0.282–0.550)	<0.01
P for trend	NA	NA	NA	NA	<0.01

Table 3	Hazard ratios	(95% confidence intervals)	) of incident diabetes	and the healthy lifestyle scores
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Adjusted for age (<45/≥45 years), gender, community, education years (≥9/<9 years), family history of diabetes (no/yes), hypertension (no/yes), dyslipidemia (no/yes).



involving 558,302 Chinese participants. It was found that compared with participants with an unhealthy lifestyle, those with a healthy lifestyle had a significantly lower risk of type 2 diabetes mellitus. The adjusted hazard ratio was 0.30 and 0.41, respectively, and 0.30 for the combined cohort. Another communitybased study involving 11,596 Chinese adults aged  $\geq$ 40 years found that the risk of diabetes in participants with a high healthy lifestyle score decreased by 32–44% when compared with participants with a low score<sup>26</sup>. Our findings showed that most of the nine healthy lifestyle factors were protective against diabetes. In addition to never smoking, never drinking, appropriate sleep time, high fruit intake, and maintaining optimal weight, low intake of edible oil and salt were also beneficial for glucose metabolism. However, a sedentary time <6 h/day and vegetable intake  $\geq$ 300 g/day had no significant protective effect. Although sedentary behavior is considered a risk factor for diabetes, some studies have reported inconsistent results. For example, a case–control study found



**Figure 4** | Hazard ratios (95% confidence intervals) associated with extreme categories (0–3 vs 7–9) of the nine healthy lifestyle factors after subtraction of one factor at a time. Adjusted for age ( $<45/\geq45$  years), gender, community, education years ( $\geq9/<9$ ), family history of diabetes (no/ yes), hypertension (no/yes), dyslipidemia (no/yes), and corresponding subtracted components.

Healthy lifestyle score	Baseline		Follow-up	Follow-up		Change in plasma glucose levels $^{\dagger}$	
	FPG	2hPG	FPG	2hPG	FPG	2hPG	
0–3	5.03 ± 0.75	5.52 ± 1.44	5.72 ± 1.80	7.11 ± 2.62	0.71 ± 1.92	1.59 ± 2.88	
4	5.04 ± 0.72	5.54 ± 1.38	5.62 ± 1.58*	6.89 ± 2.32*	0.59 ± 1.71*	1.36 ± 2.60	
5	5.03 ± 0.73	5.48 ± 1.33	5.57 ± 1.59*	6.89 ± 2.63*	0.54 ± 1.76*	1.43 ± 2.84	
6	5.07 ± 0.75	5.49 ± 1.31	5.51 ± 1.48*	6.59 ± 2.13*	0.45 ± 1.69*	1.10 ± 2.39*	
7—	5.05 ± 0.74	5.57 ± 1.25	5.42 ± 1.73*	6.64 ± 2.54*	0.38 ± 1.94*	1.04 ± 2.83*	
P value	0.539	0.360	0.001	<0.01	<0.01	<0.01	

Table 4 | The association between healthy lifestyle scores and the changes in plasma glucose levels during follow-up

\*P < 0.05, Compared with healthy lifestyle score of 0–3. <sup>†</sup>Changes in plasma glucose levels: plasma glucose levels at followed up minus plasma glucose levels at baseline. 2hPG, 2 h post-load plasma glucose; FPG, fasting plasma glucose.

that there was no significant difference in sedentary time between patients with type 2 diabetes mellitus and healthy controls after adjusting for BMI<sup>28</sup>. Another study showed that the total sedentary time was not associated with the development of gestational diabetes mellitus<sup>29</sup>. Hsuch et al. also found no significant correlation between total sedentary time and the risk of type 2 diabetes mellitus. However, after specifying sedentary behaviors, watching television  $\geq 2$  h/day was associated with a high risk of type 2 diabetes mellitus<sup>30</sup>. In our study, we did not observe that vegetable intake was associated with a lower risk of diabetes, which is inconsistent with previous studies<sup>31,32</sup>. An earlier meta-analysis showed that consuming more green leafy vegetables reduces the risk of diabetes by 14%<sup>33</sup>. However, Hamer et al.<sup>34</sup> showed that an increase in vegetable intake did not reduce the risk of diabetes. Another meta-analysis also found no association between total vegetable intake and diabetes, but intake of root vegetables was associated with a lower risk of diabetes<sup>35</sup>. A recent study also showed that vegetable intake did not alter the gut microbiota or related metabolites to reduce the risk of type 2 diabetes mellitus<sup>36</sup>. Although both

sedentary time <6 h/day and vegetable intake  $\geq$ 300 g/day were not independently associated with the development of type 2 diabetes mellitus, it was found that the risk of type 2 diabetes mellitus gradually decreased with the increase in the number of healthy lifestyle factors based on the analysis of any combination of various healthy lifestyle factors. The possible reason was that a certain healthy lifestyle factor had no significant effect on diabetes, but synergy appeared to decrease the risk of type 2 diabetes mellitus. The exact mechanism was unclear.

Interestingly, our results showed that the nine healthy lifestyle factors appeared to be more effective in preventing type 2 diabetes mellitus in men than in women. A possible reason is that the progression of diabetes in men is more susceptible to lifestyle. Previous studies have shown that there is a significant difference in the risk of diabetes between men and women. While the specific pathogenesis has not yet been elucidated, it may be related to the different levels of sex hormones, nutritional factors, and social and psychological factors<sup>37,38</sup>.

Notably, our results showed that never smoking was the strongest protective factor against type 2 diabetes mellitus among all healthy lifestyle factors. A large number of studies have demonstrated that active and passive smoking are both closely related to a higher risk of type 2 diabetes mellitus<sup>39-41</sup>. Cigarettes may change body composition, cause adverse fat distribution, reduce insulin sensitivity, and damage pancreatic βcell function, thereby affecting glucose homeostasis<sup>40</sup>. A previous study found a linear dose-response relationship between smoking and the risk of type 2 diabetes mellitus. Smoking accounted for 18.8% and 5.4% of the etiology of type 2 diabetes mellitus in men and women, respectively<sup>42</sup>. A recent cohort study in Korea showed that after adjustment for multiple factors, compared with that among current smokers, the risk of diabetes among quitters and non-smokers decreased by 14.2% and 38.4%, respectively<sup>43</sup>. Pan et al.<sup>39</sup> found that the risk of diabetes decreased with an increase in smoking cessation time among former smokers.

The major advantages of our study are the large sample size, relatively long follow-up time, and high follow-up rate. To our knowledge, this is the first study to explore the influence of nine healthy lifestyle factors on the risk of type 2 diabetes mellitus in an ethnic minority region in China. More importantly, we analyzed the importance of each lifestyle factor, and five different methods were used for the sensitivity analysis to maximize the robustness of our results.

Nevertheless, this study has several limitations. First, lifestyle factors depend on participants' self-reports; therefore, measurement errors are inevitable. Second, other lifestyle factors such as intake of red meat, milk, seafood, and beverages were not analyzed. Finally, our participants were permanent residents of Guizhou Province, China, and the results may not be applicable to other populations.

In summary, a healthy lifestyle can reduce the incidence of type 2 diabetes mellitus in adults in Guizhou, China. With the increasing number of healthy lifestyle factors, the incidence of diabetes

gradually decreased. A healthy lifestyle, especially not smoking, may be an effective way to prevent type 2 diabetes mellitus.

# ACKNOWLEDGMENTS

Funding for this study came from the Guizhou Provincial Science and Technology Fund (Contract Number: [2018]2819).

# DISCLOSURE

The authors declare no conflict of interest.

Approval of the research protocol: The study was approved by the Institutional Review Board of the Guizhou Center for Disease Control and Prevention (no. S2017-02).

Informed consent: written informed consent was obtained from all participants.

Registry and the registration no. of the study/trial: 20170314. Animal studies: N/A.

# DATA AVAILABILITY STATEMENT

Application for datasets generated during and/or analyzed during the current study may be considered by the corresponding author on reasonable request.

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# SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1 | Sensitivity analysis of the hazard ratios (95% confidence intervals) of incident diabetes with healthy lifestyle scores