# ORIGINAL ARTICLE



# Relationship between healthy lifestyle behaviors and cardiovascular risk factors in Chinese patients with type 2 diabetes mellitus: a subanalysis of the CCMR-3B STUDY

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#### Abstract

*Aims* This subanalysis of a cross-sectional, nationwide study was undertaken to assess the relationship between healthy lifestyle behaviors and multiple cardiovascular risk factors among people with type 2 diabetes mellitus (T2DM).

*Methods* Data collected from 25,454 participants, including demographics, lifestyle behaviors and cardiovascular risk profiles, were analyzed. Blood pressure control as well as blood glucose and blood lipid (3Bs) levels were measured as multi-risk factors for cardiovascular disease. Healthy lifestyle behaviors included regular exercise, nonsmoking status and no alcohol consumption. The

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relationship between the healthy lifestyle behavior(s) and control of 3B(s) was calculated.

*Results* Of the 25,454 eligible participants, 4171 (16.4%) were current smokers, 2011 (7.9%) currently consumed alcohol, and 11,174 (43.9%) did not exercise. In total, 654 (2.6%) reported all three unhealthy lifestyle behaviors. Most participants (71.1%) had received at least a high school education and were more likely to smoke and drink as compared to those with lower education. Unhealthy lifestyle behaviors were commonly found in participants with low atherosclerosis risk, such as non-elderly people and those with an above-college education level. Unhealthy lifestyle is associated with poor 3B control and worse medication adherence.

*Conclusions* Unhealthy lifestyles are common in Chinese people with T2DM, especially in people who are nonelderly and above-college educated. Interventions aimed at changing risky lifestyle behaviors are required for improved outcomes for Chinese patients with T2DM.

**Keywords** Health behaviors · Blood glucose · Blood pressure · Blood lipids · Cardiovascular risk

# Introduction

Type 2 diabetes mellitus (T2DM) is prevalent and rapidly rising in China as the population increasingly adopts a Western diet. The total number of people in China with diabetes is expected to increase to 42.3 million by 2030 [1]. The rapid growth rate in the incidence of T2DM comes at a high economic cost (loss of \$448 billion from 2006 to 2015) and with many social issues, especially given the link between diabetes, hypertension and dyslipidemia with atherosclerosis and cardiovascular disease [1]. Moreover, individuals with T2DM and uncontrolled hyperglycemia, hypertension and dyslipidemia are at even a higher risk for the development of cardiovascular disease. Thus, control of blood glucose, blood pressure and blood lipids (3Bs) will have a significant impact on long-term health outcomes for T2DM patients. In the cross-sectional, nationwide 3B STUDY conducted in China, cardiovascular risk factors were evaluated in patients with T2DM. This study confirmed that achieving adequate control of cardiovascular disease risk factors in people with T2DM remains a critical challenge in China [2].

Lifestyle changes, including dietary intake and physical exercise, remain important for the management of prediabetes as well as T2DM [3]. In the Da Qing Diabetes Prevention Study that included 577 patients with impaired glucose tolerance, lifestyle interventions, such as reducing alcohol consumption, regular exercise and consuming a vegetable-rich diet, could delay the incidence of T2DM in individuals with prediabetes [4]. In addition, regular exercise was associated with greater improvements in hemoglobin A1c (HbA1c) control in people with T2DM [5]. The beneficial impact of self-directed exercise in improving HbA1c and other outcomes was confirmed in systemic review of 28 studies of T2DM patients [6]. Another study in smokers with newly diagnosed T2DM demonstrated that smoking cessation was associated with amelioration of metabolic parameters and reduced blood pressure and albuminuria [7]. Thus, lifestyle modifications are a cornerstone strategy for successful long-term outcomes in people with T2DM.

Although the impact of lifestyle behaviors on cardiovascular disease risk is well documented, there is a paucity of data on lifestyle patterns and their consequences for people with T2DM in China. The Nationwide Assessment of Cardiovascular Risk Factors: blood glucose, blood pressure and blood lipid in Chinese patients with type 2 diabetes (3B STUDY) was designed and conducted under the guidance of the China Cardiometabolic Registries (CCMR) advisory board as a cohort study series with the aim to more fully describe the epidemiology and real-world clinical outcomes of cardiovascular and metabolic diseases in China [2]. The CCMR-3B STUDY revealed that blood glucose, blood pressure and blood lipid control were associated with lower body mass index (BMI), no current smoking or drinker, and higher education in T2DM patients in China [2]. Subsequent analysis revealed that poorer metabolic control was associated with low socioeconomic status [8] and obesity [9], as well as the underuse of the ACEI/ARB in those with hypertension in albuminuria [10]. However, to the best of our knowledge, robust evidence is lacking to support the relationship between healthy lifestyle behaviors and the control of multiple risk factors in Chinese people with T2DM. Thus, in this subanalysis of the 3B STUDY, we assessed the proportion of T2DM patients in China that adopted healthy lifestyle factors and evaluated the relationship between these behaviors and multiple cardiovascular risk factors. These results may help us to draft new public health policy and generate new research hypotheses for improving the care of T2DM patients in China.

# Materials and methods

# Study design

This is a subanalysis of the observational, cross-sectional, multicenter, multispecialty CCMR-3B STUDY of outpatients with established T2DM according to World Health Organization (WHO) criteria [11]. A total number of 25,454 participants with T2DM aged  $\geq$ 18 years were enrolled between August 2010 and March 2011 from 104 hospitals across all major geographical regions in China. The protocol of this study was approved by the Ethics Committee of Peking University People's Hospital (Ethics Number: [2010]024). All procedures were performed in accordance with the ethical standards of the institutional research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. Informed consent was obtained from all participants included in this study.

# Definition of lifestyle behaviors

Smoking status was defined as follows: (1) nonsmoker, never smoked; (2) current smoker, average of at least one cigarette daily for >1 year; (3) passive smoker, exposed to smoke for >1 year through a family member colleague, or work environment; and (4) previous smoker, quit smoking for >1 year. Alcohol consumption was defined as follows: (1) no alcohol consumption, average daily alcohol consumption <25 g alcohol; (2) current alcoholic, the average daily alcohol consumption of  $\geq 25$  g alcohol for >1 year; and (3) previous alcoholic, an alcoholic who has abstained from alcohol for >1 year. Exercise was defined as follows: (1) no exercise, the absence of exercise; (2) frequent exercise, >30 min of exercise training >3 times a week; (3) pro re nata (PRN; i.e., as needed), >30 min of exercise training >1 to <3 times a week; (4) few exercise, >30 min of exercise training  $\leq 1$  time per week; and (5) no or less exercise, no exercise + PRN exercise + few exercise. For this study, >30 min of exercise training was the equivalent of brisk walking.

T2DM patients that were considered to have healthy lifestyle behaviors had all of the following criteria:

(1) current nonsmoking status, including nonsmokers, previous smoker and passive smokers; (2) current nondrinkers, including those without alcohol consumption and previous alcoholics; and (3) frequently exercise. T2DM patients were considered to have unhealthy lifestyle behaviors if they met all of the following criteria: (1) current smoker, (2) current alcoholic, and (3) no or less exercise.

Target goals of 3Bs were defined as follows: HbA1c <77 mmol/mol (7%), blood pressure <140/80 mmHg and total cholesterol <4.5 mmol/L. These target goals are consistent with the 2013 Chinese guidelines for prediabetes prevention and treatment [12].

#### **Data collection**

Patient data were collected from medical charts and clinical examinations (i.e., anthropometry, blood pressure, blood glucose and blood lipid measurements) conducted at one outpatient visit. Face-to-face interviews were also conducted to obtain the following information: health behavior status (i.e., smoking status, alcohol consumption and exercise intensity), current medication use and personal history of hypertension and major cardiovascular diseases. Fasting serum glucose, total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and triglycerides (TG) were measured at each study site with an automated analyzer. HbA1c data were obtained within 3 months prior to the enrollment visit or at enrollment.

#### Statistical analysis

Continuous variables are expressed as the mean  $\pm$  SD and were analyzed using Student's t test for normally distributed data. Categorical variables were expressed as numbers (%) and analyzed using the Chi-squared and Fisher's exact tests. HbA1c measurements were reported in IFCC units (mmol/mol) and followed by NGSP units (%). Multivariate logistic regression analysis was conducted to identify associations between dependent and independent variables. Variables with P < 0.2 in univariate analyses were included in the multivariate phase. Only variables with P < 0.1 remained in the final model after the application of a backward elimination variable selection procedure. Adjusted odds ratios with 95% confidence intervals (CIs) were reported. Statistical analyses were conducted using SAS version 9.2 (SAS Institute Inc., Cary, NC, USA). All enrolled people were identified by participant numbers in the database to ensure anonymity. All artwork was created by GraphPad Prism 5 (San Diego, CA, USA).

#### Results

#### **Patient characteristics**

As shown in Table 1, the mean age of the 25,454 participants with T2DM was  $62.6 \pm 11.9$  years with a mean BMI of  $24.8 \pm 3.6$  and waist circumference of 83.5 cm. Patients had T2DM for a mean of  $8.1 \pm 6.83$  years, and most had good medication adherence.

Analysis of the patient characteristics by smoking, alcohol consumption or exercise status was next undertaken. As shown in Table 2, 4171 (16.4%) participants were current smokers, 2011 (7.9%) were current drinkers, and 11,174 (43.9%) did not exercise. In addition, 654 (0.3%) participants smoke, drank and did not exercise; 11,697 (45.9%) participants adopted a healthy lifestyle (i.e., no smoking/drinking and regular exercise). People currently smoking or consuming alcohol tended to be

Table 1 Participant characteristics

Variables	Participants $(n = 25,454)$
Age (year), mean $\pm$ SD	$62.6 \pm 11.9$
<65, n (%)	13,855 (54.4)
≥65, <i>n</i> (%)	11,599 (45.6)
Gender-male, n (%)	11,955 (47.0)
BMI (kg/m <sup>2</sup> ), mean $\pm$ SD	$24.8\pm3.57$
<24 kg/m <sup>2</sup>	10,619 (41.7)
24–28 kg/m <sup>2</sup>	10,664 (41.9)
$\geq 28 \text{ kg/m}^2$	4171 (16.4)
Waist circumference (cm), mean $\pm$ SD	$83.5\pm8.10$
Residence-urban, $n$ (%)	22,776 (89.5)
Education	
Illiteracy, n (%)	1695 (6.7)
Primary education, $n$ (%)	5667 (22.3)
Secondary education, $n$ (%)	11,936 (46.9)
College and above, $n$ (%)	6156 (24.2)
Diabetes duration (year)	$8.1 \pm 6.83$
Medical insurance	
Yes, <i>n</i> (%)	23,650 (92.9)
No, <i>n</i> (%)	1804 (7.1)
Income (CNY/month)	
<2000, n (%)	10,039 (39.4)
2000–5000, n (%)	11,586 (45.5)
≥5000, <i>n</i> (%)	2964 (11.6)
Unknown, n (%)	865 (3.4)
Medication adherence	
Good, <i>n</i> (%)	22,056 (86.7)
Poor, <i>n</i> (%)	3398 (13.4)

Variables	Smoking		p value	Alcohol consumption	umption	p value	Exercise <sup>b</sup>		d	Healthy behavior <sup>c</sup>	ior <sup>c</sup>	p value
	Current $(n = 4171)$	$No^{a}$ ( <i>n</i> = 21,283)		Current $(n = 2011)$	$No^{a}$ ( <i>n</i> = 23,443)		Frequently $(n = 14,280)$	No/less $(n = 11, 174)$		Yes $(n = 11, 697)$	Totally unhealthy $(n = 654)$	
Age (year), mean $\pm$ SD <65, $n$ (%)	$56.6 \pm 11.8$ 3125 (74.9)	$63.8 \pm 11.6$ 10,730 (50.4)	<0.001 <0.001	56.2 ± 11.6 1535 (76.3)	$63.1 \pm 11.7$ 12,320 (52.6)	<0.001 <0.001	$61.9 \pm 11.0$ 8215 (57.5)	$63.5 \pm 12.92$ 5640 (50.5)	<0.001 <0.001	$62.8 \pm 10.7$ 6306 (53.9)	$53.7 \pm 11.9$ 531 (81.2)	<0.001 <0.001
≥65, n (%)	1046 (25.1)	10,553 (49.6)		476 (23.7)	11,123 (47.5)		6065 (42.5)	5534 (49.5)		5391 (46.1)	123 (18.8)	
Gender-male, $n$ (%)	3888 (93.2)	8067 (37.9)	<0.001	1944 (96.7)	10,011 (42.7)	<0.001	6685 (46.8)	5270 (47.2)	0.579	4258 (36.4)	641 (98.0)	<0.001
BMI (kg/m <sup>2</sup> ), mean $\pm$ SD	$25.1\pm3.32$	$24.8\pm3.62$	<0.001	$25.4 \pm 3.37$	$24.8\pm3.58$	<0.001	$24.7 \pm 3.43$	$25.0\pm3.75$	<0.001	$24.7 \pm 3.49$	$25.6\pm3.51$	<0.001
<24 kg/m <sup>2</sup>	1527 (36.6)	9092 (42.7)	<0.001	643 (32.0)	9976 (42.6)	<0.001	6056 (42.4)	4563 (40.8)	<0.001	5135 (43.9)	208 (31.8)	<0.001
24–28 kg/m <sup>2</sup>	1940 (46.5)	8724 (41.0)		970 (48.2)	9694 (41.4)		6119 (42.9)	4545 (40.7)		4856 (41.5)	309 (47.3)	
$\geq 28 \text{ kg/m}^2$	704 (16.9)	3467 (16.3)		398 (19.8)	3773 (16.1)		2105 (14.74)	2066 (18.5)		1706 (14.6)	137 (21.0)	
Waist circumference (cm), mean ± SD	87.3 ± 7.81	$82.6 \pm 7.90$	<0.001	$88.1 \pm 7.36$	$83.0 \pm 8.02$	<0.001	83.6 ± 7.89	$83.4 \pm 8.37$	0.149	82.5 土 7.63	87.7 土 7.65	<0.001
Residence-urban, $n$ (%)	3709 (88.9)	19,067 (89.6)	0.201	1802 (89.6)	20,974 (89.5)	0.845	12,772 (89.4)	10,004 (89.5)	0.817	10,460 (89.4)	583 (89.1)	0.820
Education			< 0.001			<0.001			<0.001			<0.001
Illiteracy, $n(\%)$	108 (2.59)	1587 (7.46)		51 (2.54)	1644 (7.01)		702 (4.92)	993 (8.89)		650 (5.56)	18 (2.75)	
Primary education, $n$ (%)	592 (14.2)	5075 (23.9)		271 (13.5)	5396 (23.0)		2803 (19.6)	2864 (25.6)		2452 (21.0)	81 (12.4)	
Secondary education, $n$ (%)	2157 (51.7)	9779 (46.0)		964 (48.0)	10,972 (46.8)		7014 (49.1)	4922 (44.1)		5695 (48.7)	326 (49.9)	
College and above, $n$ (%)	1314 (31.5)	4842 (22.8)		725 (36.1)	5431 (23.2)		3761 (26.3)	2395 (21.4)		2900 (24.8)	229 (35.0)	
Diabetes duration(y)	$6.8\pm6.08$	$8.3\pm6.95$	<0.001	$6.8\pm5.83$	$8.2\pm6.90$	<0.001	$7.8\pm6.56$	$8.5\pm7.15$	<0.001	$8.0\pm6.64$	$6.3\pm5.43$	<0.001
Medical insurance			0.001			0.161			<0.001			0.016
Yes, n (%)	3824 (91.7)	19,826 (93.2)		1853 (92.1)	21,797 (93.0)		13,372 (93.6)	10,278 (92.0)		10,971 (93.8)	598 (91.4)	
No, $n$ (%)	347 (8.32)	1457 (6.85)		158 (7.86)	1646 (7.02)		908 (6.36)	896 (8.02)		726 (6.21)	56 (8.56)	
Home revenue			<0.001			<0.001			0.001			<0.001
(CNY/month)												
<2000, n (%)	1445 (34.6)	8594 (40.4)		619 (30.8)	9420 (40.2)		5738 (40.2)	4301 (38.5)		4828 (41.3)	178 (27.2)	
2000–5000, n (%)	1910 (45.8)	9676 (45.5)		981 (48.8)	10,605 (45.2)		6488 (45.4)	5098 (45.6)		5302 (45.3)	346 (52.9)	
$\geq$ 5000, <i>n</i> (%)	669 (16.0)	2295 (10.8)		358 (17.8)	2606 (11.1)		1566 (11.0)	1398 (12.5)		1173 (10.0)	113 (17.3)	
Unknown, $n$ (%)	147 (3.52)	718 (3.37)	100 0	53 (2.64)	812 (3.46)	100 0	488 (3.42)	377 (3.37)	100 0	394 (3.37)	17 (2.60)	
Medication adherence			<0.001			<0.001			<0.001			<0.001

Table 2 Participant characteristics by smoking, alcohol consumption, exercise and healthy behavior status

Variables	Smoking		<i>p</i> value	value Alcohol consumption	umption	p value	<i>p</i> value Exercise <sup>b</sup>		d	Healthy behavior <sup>c</sup>	/ior <sup>c</sup>	<i>p</i> value
	Current $(n = 4171)$	Current $No^{a}$ ( <i>n</i> = 4171) ( <i>n</i> = 21,283)		Current $(n = 2011)$	Current $No^{a}$ ( <i>n</i> = 2011) ( <i>n</i> = 23,443)		Frequently No/less $(n = 14,280)$ $(n = 11)$	Frequently No/less $(n = 14,280)$ $(n = 11,174)$		YesTotally $(n = 11, 697)$ unhealthy $(n = 654)$	Totally unhealthy $(n = 654)$	
Good, $n$ (%)	3294 (79.0) 18,762 (88.2)	18,762 (88.2)		1514 (75.3) 20,542 (87.6)	20,542 (87.6)		12,646 (88.6)	9410 (84.2)		10,521 (90.0)	454 (69.4)	
Poor, $n$ (%)	877 (21.0)	877 (21.0) 2521 (11.9)		497 (24.7) 2901 (12.4)	2901 (12.4)		1634 (11.4) 1764 (15.8)	1764 (15.8)		1176 (10.1) 200 (30.6)	200 (30.6)	
BMI body mass index												
<sup>a</sup> Includes previous smoking or drinking history	ig or drinking hi	istory										
<sup>b</sup> Exercise lifestyle refers to frequently exercise	o frequently exe	sreise										
<sup>c</sup> Healthy behavior refers to no current smoking or alcohol consumption and regular exercise; totally unhealthy behavior refers to current smoking and alcohol consumption and no or occasional	o no current smol	king or alcohol cc	nsumptio	n and regular e	exercise; totally u	unhealthy	behavior refers	to current smokir	ng and a	alcohol consumpt	ion and no or c	ccasional

exercise

**Fable 2** continued

subgroups vounger than the other (smoking.  $56.6 \pm 11.8$  years vs.  $63.8 \pm 11.6$  years, P = 0.0001;  $56.2 \pm 11.6$  years drinking, VS.  $63.1 \pm 11.7$  years, P < 0.001). Moreover, most of the participants currently smoking (93.2%) or consuming alcohol (96.7%) were male. People who smoked, consumed alcohol or did not exercise tended to have a greater BMI than those who had a healthy lifestyle (all, P < 0.001; Table 2). Furthermore, participants who had received at least a high school education were more likely to smoke and drink than those with less education (smoking, 83.2% vs. 16.8%, P < 0.001; drinking, 84% vs. 16%, P < 0.001). Finally, 30.6% of people with unhealthy lifestyles had poor medication adherence as compared to only 10.1% of those with healthy lifestyles (P < 0.001).

# Pharmaceutical treatment by healthy lifestyle behaviors

The pharmaceutical treatment patterns of the participants are described in Table 3. Slightly more than half of the participants (55.0%) were treated with oral hypoglycemic drugs (OHD) alone. Another 18.2% were treated with OHD in combination with insulin; and 17.5% were treated with insulin alone. Calcium channel blockers were the most commonly reported antihypertensive drugs used (24.4%), following by Ang II receptor antagonists (16.0%) and angiotensin-converting enzyme inhibitors (8.33%). In addition, 19.9% of participants received treatment with statins, and 18.44% of participants were being treated with aspirin. A greater proportion of current smokers and drinkers and those with no/less exercise used as compared to those with healthy lifestyle behaviors (all,  $P \le 0.019$ ; Table 3).

# **3B** control

Achievement of 3B targets (i.e., blood glucose, blood lipids and blood pressure) is shown in Fig. 1. The mean HbA1c was 83 mmol/mol (7.6%), and nearly half (44.9%) of the participants reached the recommended target goal for adequate glycemic control (HbA1c < 77 mmol/mol, or 7.0%; Supplemental Table 1). Only 35.6, 35.0 and 41.7% of participants classified as current smokers, current drinkers and those participating in no or less exercise reached this therapeutic goal, respectively, which was significantly less than those with healthy behaviors (all, P < 0.001).

The mean systolic and diastolic blood pressure (SBP and DBP, respectively) was 133 and 78.8 mmHg, respectively (Supplemental Table 1). Overall, 40.7% of participants reached the recommended target goal for adequate blood pressure control (SBP < 140 and DBP < 80 mmHg); however, only 38, 35.1 and 39.5% of current smokers,

Table 3 Treatment patterns by smoking, alcohol consumption,	it patterns by sn	oking, alcoho	-	exercise a	nd healthy be	exercise and healthy behavior status		ء ډ		-			-
Variables, $n$ (%)	All	Smoking		<i>p</i> value	Alcohol consumption	sumption	<i>p</i> value	Exercise		<i>p</i> value	Healthy behavior	ior	<i>p</i> value
	participants $(n = 25,454)$	Current $(n = 4171)$	$No^{a}$ ( <i>n</i> = 21,283)		Current $(n = 2011)$	$No^{a}$ ( <i>n</i> = 23,443)		Frequently $(n = 14,280)$	No/less $(n = 11, 174)$		Yes ( <i>n</i> = 11,697)	Totally unhealthy $(n = 654)$	
OHD only	13,988 (54.6)	2118 (50.8)	11,870 (55.8)	<0.001	1029 (51.2)	12,959 (55.3)	0.001	8184 (57.3)	5804 (51.9)	<0.001	6792 (58.1)	301 (46.0)	<0.001
Sulfonylureas	6578 (47.0)	981 (46.3)	5597 (47.2)	0.480	476 (46.3)	6102 (47.1)	0.942	3769 (46.1)	2809 (48.4)	0.006	3137 (46.2)	135 (44.9)	0.649
Biguanide	7623 (54.5)	1264 (59.7)	6359 (53.6)	<0.001	619 (60.2)	7004 (54.1)	< 0.001	4495 (54.9)	3128 (53.9)	0.228	3664 (54.0)	176 (58.5)	0.123
∞-glucosidase inhibitor	4432 (31.7)	582 (27.5)	3850 (32.4)	<0.001	323 (31.4)	4109 (31.7)	0.833	2539 (31.0)	1893 (32.6)	0.046	2143 (31.6)	81 (26.9)	0.089
Thiazolidinediones	1378 (9.9)	211 (10.0)	1167 (9.8)	0.850	100 (9.7)	1278 (9.9)	0.882	875 (10.7)	503 (8.7)	<0.001	734 (10.8)	28 (9.3)	0.409
Meglitinides	1146 (8.2)	165 (7.8)	981 (8.7)	0.460	85 (8.3)	1061 (8.2)	0.934	726 (8.9)	420 (7.2)	0.001	615 (9.1)	22 (7.3)	0.300
DPP-4 inhibitor	44 (0.31)	4 (0.19)	40 (0.34)	0.262	3 (0.29)	41 (0.32)	1.000	23 (0.28)	21 (0.36)	0.401	19 (0.28)	0	1.000
GLP-1 analogue	11 (0.08)	0	11 (0.09)	0.203	3 (0.29)	8 (0.06)	0.042	5 (0.06)	6 (0.10)	0.567	4 (0.06)	0	1.000
Insulin only	4446 (17.5)	791 (19.0)	3655 (17.2)	<0.001	349 (17.4)	4097 (17.5)	0.001	2174 (15.2)	2272 (20.3)	0.000	1754 (15.0)	147 (22.5)	< 0.001
OHD + insulin	4620 (18.2)	813 (19.5)	3807 (17.9)	0.014	404 (20.1)	4216 (18.0)	0.019	2562 (17.9)	2058 (18.4)	0.328	2067 (17.7)	136 (20.8)	0.042
Antihypertensive agents													
ACE inhibitor	2121 (8.3)	355 (8.5)	1766 (8.3)	0.684	167 (8.3)	1954 (8.3)	0.962	1152 (8.1)	969 (8.7)	0.083	916 (7.8)	47 (7.2)	0.550
Ang II receptor antagonist	4084 (16.0)	523 (12.5)	3561 (16.7)	<0.001	282 (14.0)	3802 (16.2)	0.010	2081 (14.6)	2003 (17.9)	<0.001	1784 (15.3)	96 (14.7)	0.691
Calcium channel blockers	6202 (24.4)	781 (18.7)	5421 (25.5)	<0.001	414 (20.6)	5788 (24.7)	<0.001	3429 (24.0)	2773 (24.8)	0.138	2913 (24.9)	125 (19.1)	0.001
Beta-blocker	2361 (9.3)	319 (7.7)	2042 (9.6)	<0.001	147 (7.3)	2214 (9.4)	0.002	1210 (8.5)	1151 (10.3)	<0.001	1011 (8.6)	45 (6.9)	0.117
Lipid modulating agents													
Statins	5054 (19.9)	830 (19.9)	4224 (19.9)	0.938	401 (19.9)	4653 (19.9)	0.921	2686 (18.8)	2368 (21.2)	<0.001	2195 (18.8)	143 (21.9)	0.051
Aspirin	4693 (18.4)	791 (19.0)	3902 (18.3)	0.337	418 (20.8)	4275 (18.2)	0.005	2509 (17.6)	2184 (19.6)	<0.001	2028 (17.3)	144 (22.0)	0.002
OHD Oral hypoglycemic drug, ACE angiotensin-converting en <sup>a</sup> Includes mevious smoking or drinking history	ycemic drug, AC s smokino or dr	7E angiotensin inking history	1-converting enz	yme, DPF	dipeptidyl p	zyme, DPP dipeptidyl peptidase, GLP g	glucagon-l	glucagon-like peptide					
<sup>b</sup> Exercise lifestyle refers to frequently exercise	e refers to freque	ently exercise											
<sup>c</sup> Healthy behavior refers to no current smoking or alcohol consumption and regular exercise; totally unhealthy behavior refers to current smoking and alcohol consumption and no or occasional exercise.	r refers to no cur	rent smoking (	or alcohol consu	umption an	d regular exe	rcise; totally unl	realthy bel	navior refers to	current smoking	and alcoh	iol consumption	and no or oc	casional
AAUUUV													

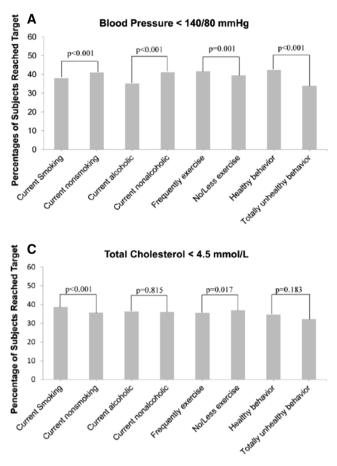


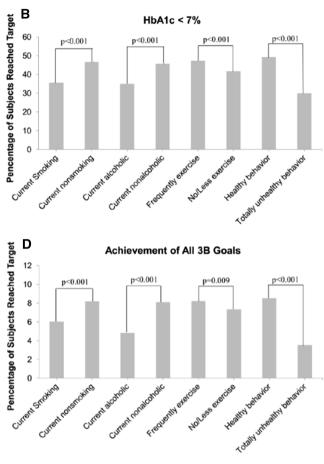
Fig. 1 Achievement of 3B targets in Chinese T2DM patients by healthy lifestyle behaviors. Achievement of **a** blood pressure, **b** HbA1c, **c** total cholesterol and **d** all 3B targets was compared in

current drinkers and those participating in no or less exercise reached this therapeutic goal, respectively, which was lower than that observed in patients with healthy behaviors (all,  $P \le 0.001$ ).

The mean total serum cholesterol was 5.0 mmol/L with 36.1% of participants reaching the recommended target goal (total cholesterol <4.5 mmol/L; Supplemental Table 1). Only 7.84% of the participants achieved the recommended target goal for adequate HbA1c, blood pressure and total cholesterol control. Moreover, a greater proportion of those with only healthy behaviors achieved the 3B(s) goals as compared to those with no healthy behaviors (42.4 vs. 33.9%, respectively, for blood pressure, P < 0.001; 49.2 vs. 30.0%, respectively, for blood glucose, P < 0.001; and 8.5 vs. 3.5%, respectively, for all 3B targets, P < 0.001).

#### Factors related to 3B achievement

Multivariate logistic regression analysis was next undertaken to analyze the relationship between lifestyle



T2DM patients that smoked, drank alcohol and/or abstained from exercise with patients that had healthy lifestyle behaviors

behaviors and reaching 3B targets after adjustment for age, gender, BMI, smoking, alcohol consumption, exercise and the diabetes duration (Fig. 2). As shown in Supplementary Table 2, current smoking, current drinking and frequent exercise were strongly negatively correlated with both achievement of the HbA1c target (current smoking, OR = 0.71, P < 0.001; current drinking, OR = 0.83, P < 0.001; and frequent exercise, OR = 1.51, P < 0.001) and achievement of all 3Bs goals (current smoking, OR = 0.72, P < 0.001; current drinking, OR = 0.73, P < 0.001; and frequent exercise, OR = 1.44, P < 0.001).

#### Discussion

Because few studies have analyzed lifestyle patterns and their outcomes for people with T2DM in China, this subanalysis of the 3B STUDY was performed to evaluate the proportion of T2DM patients in China that adopted healthy lifestyle factors and assess the relationship between these behaviors and multiple cardiovascular risk factors.

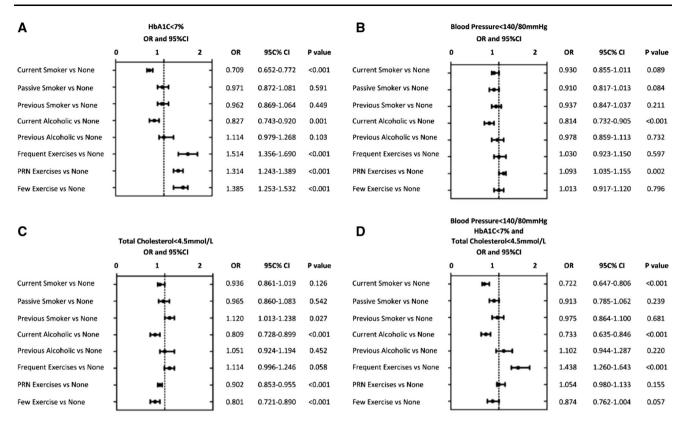


Fig. 2 Factors related to 3B achievement. Odds ratios (ORs) and 95% confidence intervals (95% CI) for achievement of **a** blood pressure, **b** HbA1c, **c** total cholesterol and **d** all 3B targets in Chinese T2DM patients

We demonstrated that unhealthy lifestyles are common in Chinese people with T2DM. Unexpectedly, unhealthy lifestyle behaviors were commonly found in participants with low atherosclerosis risk, such as younger and middleaged people and those with an above-college education level. Furthermore, an unhealthy lifestyle was associated with poor 3B control, and this population tended to have worse medication adherence. To the best of our knowledge, this is the first study focusing on healthy lifestyle behaviors and their impact on cardiovascular risk control in Chinese T2DM patients.

According to the WHO, worldwide the prevalence of tobacco smoking and alcohol consumption among adults is 22 and 62%, respectively, and about 23% of adults are insufficiently physically active [13]. Another study showed that the prevalence of alcohol consumption was 30.4% in people with T2DM [14]. In the USA, the smoking prevalence among people with diabetes and impaired fasting glucose was 25.7 and 24.2%, respectively, which was comparable with those without diabetes [15]. In the present study, 16.4% of participants with T2DM were current smokers, 7.9% were current drinkers, and 43.9% participants did not regularly exercise. Thus, unhealthy lifestyles are still common in Chinese people with T2DM. Our data also found that people who were non-elderly and above-

college educated tended to adopt more unhealthy lifestyles, which is consistent with a previous study reporting that smoking is most prevalent among the highly educated in Mexico [16]. Furthermore, younger age, male sex and full-time work were independent factors for smoking in Taiwan [17]. The authors suggested that link between socioeconomic status and smoking was related to increases in tobacco taxes [17]. In the present study, 31.5% of current smokers and 36% of current drinkers had a college education or higher. This is particularly alarming as previous epidemiological studies and diabetes education programs have often ignored this population as poor education has been identified as a risk factor of T2DM in rural Chinese [18]. Taken together, education level may not always equate with diabetes education level.

In 2013, the Chinese guidelines for the prevention and treatment of T2DM were updated to include a change in the target SBP level from 130 to 140 mmHg, similar to the American Diabetes Association (ADA) guidelines [12, 19]. According to this guideline, all people with T2DM should be advised not to smoke or use tobacco products and should be encouraged to perform at least 150 min/week of moderate-intensity aerobic physical activity. Alcohol consumption is not recommended; and if adults with diabetes choose to drink alcohol, they should be advised to do so in

moderation. Our data revealed gaps between real-world disease control patterns and clinical guidelines, especially in non-elderly and above-college-educated individuals. Youth and middle-aged people are the major targets in strategies to prevent atherosclerosis and cardiovascular events in people with T2DM. Our data strongly argue for more focus on lifestyle interventions in these populations.

As expected, our study also found that an unhealthy lifestyle (i.e., current smoking, alcohol consumption and lack or exercise) is associated with poor 3B control. Smoking is a well-known risk factor for atherosclerosis and cardiovascular disease. Smoking was also one of the strongest predictors of glycemic control in T2DM people [20]. A cross-sectional study demonstrated that the prevalence of T2DM was significantly increased after age 35 years in smokers [21]. Similarly, smoking was associated with increased T2DM risk in middle-age and elderly Chinese men [22]. Furthermore, smoking cessation predicts amelioration of microalbuminuria in people newly diagnosed with T2DM [7]. In the present study, current smoking was strongly negatively correlated with both the achievement of the HbA1c and 3B control, while passive smoking showed no correlation with 3B control.

Unlike smoking, it is generally believed that drinking alcohol is less harmful to people with T2DM, and moderate alcohol consumption is permitted in this population [23]. Light to moderate alcoholic consumption may be associated with a lower risk of T2DM [22, 24, 25]. In fact, drinking alcohol has a U-shaped relationship with metabolic syndrome and diabetes [26]. Nevertheless, a study in Japan demonstrated that excessive alcohol intake is associated with a higher risk of contracting metabolic syndrome through an increase of blood pressure and triglycerides in people with diabetes mellitus [27]. Furthermore, alcohol consumption can impair glucose counter regulation during acute insulininduced hypoglycemia [28]. In our study, fewer people who drank excessively reached HbA1c and blood pressure goals as compared to nondrinkers, and excessive drinking was strongly negatively correlated with achievement of blood glucose, blood pressure and blood lipids goals.

Physical activity is extremely important in the management of diabetes and prediabetes. According to previous study, regular physical exercise can prevent T2DM in a highrisk population [29–31] and improve blood glucose control in people with T2DM [5]. Regular physical exercise was also associated with lower HbA1c in children and adolescents with T2DM [32]. Physical activity can also improve blood pressure control, lipid profiles and fitness as well as slow the decline in mobility [33–35]. Physically active T2DM patients also have lower cardiovascular risk and vascular health [36]. In our study, people who regularly exercised showed better achievement of HbA1c and blood pressure goals than those who infrequently exercised. In the present study, we also found that people with unhealthy lifestyles tended to have worse medication adherence than those who adopted a healthy lifestyle. Although non-adherence is a major factor that can lead to morbidity and mortality in people with T2DM, the level of adherence to anti-diabetic medication and physical activity is not satisfactory as shown in previous studies [37–39]. These findings, to a certain extent, may explain why there is a relationship between unhealthy lifestyle behaviors and poor 3B control. Moreover, in our study, a higher proportion of people with unhealthy lifestyles were treated with insulin than those with healthy lifestyles. It is well known that adherence to insulin therapy is generally poor [40]. Increased provision of health education may improve medication adherence and 3B control in this population.

We also found that 98% of those with unhealthy lifestyles were male, which may be due to gender gaps between the lifestyle metrics, particularly in alcohol consumption and smoking status. Epidemiological analysis of the prevalence of alcohol consumption in China found that 16.1% of male and 2.5% of female drinkers drank at least once per day [41]. In a study conducted by the World Health Organization, 61% of men in China were reported to be current smokers compared to 4.2% of women [42]. The gender gap in smokers has been attributed to social disapproval, socioeconomic gender gaps [42], as well as influence of family and friends who smoked [43]. Given that Chinese male adults that smoke are also less likely to engage in healthy lifestyle behaviors, including a consuming healthy diet and exercise, and more likely to engage in binge drinking [44], it is possible that the engaging in one unhealthy lifestyle behavior leads to adoption of others.

Although the patient population included in the present subanalysis study was a nationally representative sample of 25,454 people from 104 hospitals across all major geographical regions in China, it is limited by its observational, cross-sectional and retrospective design. Thus, the long-term influence of health behaviors on cardiovascular outcomes could not be assessed. Furthermore, the impact of a more gender-neutral metric, including diet control, was not determined, and data related to the occupations of the participants were not collected. Thus, further longitudinal, prospective analysis will be required.

# Conclusion

Unhealthy lifestyle behaviors were found to be common in Chinese people with T2DM in the CCMR-3B STUDY, especially in people who are non-elderly and highly educated. Health behaviors, such as abstaining from cigarettes and alcohol and regular exercise, improve the factors related to 3B achievement. Thus, interventions to change risky lifestyle behaviors are crucial for optimization of outcomes for Chinese patients with T2DM.

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#### Compliance with ethical standards

**Conflict of interest** The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

**Human and animal rights disclosure** The protocol of this study was approved by the Ethics Committee of Peking University People's Hospital (Ethics Number: [2010]024). All procedures were performed in accordance with the ethical standards of the institutional research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

**Informed consent** Informed consent was obtained from all participants included in this study.

### References

- Li MZ, Su L, Liang BY et al (2013) Trends in prevalence, awareness, treatment, and control of diabetes mellitus in mainland china from 1979 to 2012. Int J Endocrinol 2013:753150. doi:10.1155/2013/753150
- Ji L, Hu D, Pan C et al (2013) Primacy of the 3B approach to control risk factors for cardiovascular disease in type 2 diabetes patients. Am J Med 126(925):e911–e922. doi:10.1016/j.amjmed. 2013.02.035
- Marin-Penalver JJ, Martin-Timon I, Sevillano-Collantes C, Del Canizo-Gomez FJ (2016) Update on the treatment of type 2 diabetes mellitus. World J Diabetes 7:354–395. doi:10.4239/wjd. v7.i17.354
- 4. Li G, Zhang P, Wang J et al (2008) The long-term effect of lifestyle interventions to prevent diabetes in the China Da Qing Diabetes Prevention Study: a 20-year follow-up study. Lancet 371:1783–1789. doi:10.1016/S0140-6736(08)60766-7
- Boule NG, Haddad E, Kenny GP, Wells GA, Sigal RJ (2001) Effects of exercise on glycemic control and body mass in type 2 diabetes mellitus: a meta-analysis of controlled clinical trials. JAMA 286:1218–1227
- 6. Byrne H, Caulfield B, De Vito G (2016) Effects of self-directed exercise programmes on individuals with type 2 diabetes mellitus: a systematic review evaluating their effect on HbA1c and other metabolic outcomes, physical characteristics, cardiorespiratory fitness and functional outcomes. Sports Med. doi:10.1007/ s40279-016-0593-y
- Voulgari C, Katsilambros N, Tentolouris N (2011) Smoking cessation predicts amelioration of microalbuminuria in newly diagnosed type 2 diabetes mellitus: a 1-year prospective study. Metab Clin Exp 60:1456–1464. doi:10.1016/j.metabol.2011.02. 014
- Tao X, Li J, Zhu X et al (2016) Association between socioeconomic status and metabolic control and diabetes complications: a cross-sectional nationwide study in Chinese adults with type 2

diabetes mellitus. Cardiovasc Diabetol 15:61. doi:10.1186/ s12933-016-0376-7

- Zhou X, Ji L, Ran X et al (2016) Prevalence of obesity and Its influence on achievement of cardiometabolic therapeutic goals in chinese type 2 Diabetes patients: an analysis of the nationwide, cross-sectional 3B study. PLoS ONE 11:e0144179. doi:10.1371/ journal.pone.0144179
- Xie Q, Hao CM, Ji L et al (2015) ACEI/ARB underused in patients with type 2 diabetes in Chinese population (CCMR-3B study). PLoS ONE 10(2):e0116970. doi:10.1371/journal.pone. 0116970
- Alberti KG, Zimmet PZ (1998) Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. Diabet Med J Br Diabet Assoc 15:539–553. doi:10.1002/(SICI)1096-9136(199807)15:7<539:AID-DIA668>3. 0.CO;2-S
- Diabetes CSO (2014) China guideline for type 2 diabetes (2013). Chin J Diabetes Mellit 6:447–498
- 13. Organization WH. http://www.whoint/gho/ncd/risk\_factors/en/
- Blomster JI, Zoungas S, Chalmers J et al (2014) The relationship between alcohol consumption and vascular complications and mortality in individuals with type 2 diabetes. Diabetes Care 37:1353–1359. doi:10.2337/dc13-2727
- Clair C, Meigs JB, Rigotti NA (2013) Smoking behavior among US adults with diabetes or impaired fasting glucose. Am J Med 126(541):e515–e548. doi:10.1016/j.amjmed.2012.11.029
- Christopoulou R, Lillard DR, Balmori de la Miyar JR (2013) Smoking behavior of Mexicans: patterns by birth-cohort, gender, and education. Int J Public Health 58:335–343. doi:10.1007/ s00038-012-0376-7
- Liu X, Li Y, Li L et al (2016) Prevalence, awareness, treatment, control of type 2 diabetes mellitus and risk factors in Chinese rural population: the RuralDiab study. Sci Rep 6:31426. doi:10. 1038/srep31426
- Tsai LT, Lo FE, Yang CC et al (2016) Influence of socioeconomic factors, gender and indigenous status on smoking in Taiwan. Int J Environ Res Public Health 13(11):E1044
- American Diabetes A (2014) Standards of medical care in diabetes–2014. Diabetes Care 37(Suppl 1):S14–S80. doi:10.2337/ dc14-S014
- 20. Bott U, Jorgens V, Grusser M, Bender R, Muhlhauser I, Berger M (1994) Predictors of glycaemic control in type 1 diabetic patients after participation in an intensified treatment and teaching programme. Diabet Med J Br Diabet Assoc 11:362–371
- Jankowich M, Choudhary G, Taveira TH, Wu WC (2011) Age-, race-, and gender-specific prevalence of diabetes among smokers. Diabetes Res Clin Pract 93:e101–e105. doi:10.1016/j.diabres. 2011.05.029
- 22. Shi L, Shu XO, Li H et al (2013) Physical activity, smoking, and alcohol consumption in association with incidence of type 2 diabetes among middle-aged and elderly Chinese men. PLoS ONE 8:e77919. doi:10.1371/journal.pone.0077919
- American Diabetes A (2015) (4) Foundations of care: education, nutrition, physical activity, smoking cessation, psychosocial care, and immunization. Diabetes Care 38(Suppl):S20–S30. doi:10. 2337/dc15-S007
- 24. Sato KK, Hayashi T, Harita N et al (2012) Relationship between drinking patterns and the risk of type 2 diabetes: the Kansai Healthcare Study. J Epidemiol Community Health 66:507–511. doi:10.1136/jech.2010.109777
- Wannamethee SG, Camargo CA Jr, Manson JE, Willett WC, Rimm EB (2003) Alcohol drinking patterns and risk of type 2 diabetes mellitus among younger women. Arch Intern Med 163:1329–1336. doi:10.1001/archinte.163.11.1329

- 26. Clerc O, Nanchen D, Cornuz J et al (2010) Alcohol drinking, the metabolic syndrome and diabetes in a population with high mean alcohol consumption. Diabet Med J Br Diabet Assoc 27:1241–1249. doi:10.1111/j.1464-5491.2010.03094.x
- Wakabayashi I (2011) Association between alcohol drinking and metabolic syndrome in Japanese male workers with diabetes mellitus. J Atheroscler Thromb 18:684–692
- 28. Avogaro A, Beltramello P, Gnudi L et al (1993) Alcohol intake impairs glucose counterregulation during acute insulin-induced hypoglycemia in IDDM patients. Evidence for a critical role of free fatty acids. Diabetes 42:1626–1634
- 29. Knowler WC, Barrett-Connor E, Fowler SE et al (2002) Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 346(6):393–403. doi:10.1056/ NEJMoa012512
- 30. Tuomilehto J, Lindstrom J, Eriksson JG et al (2001) Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med 344:1343–1350. doi:10.1056/NEJM200105033441801
- 31. Pan XR, Li GW, Hu YH et al (1997) Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and Diabetes Study. Diabetes Care 20:537–544
- 32. Herbst A, Kapellen T, Schober E et al (2015) Impact of regular physical activity on blood glucose control and cardiovascular risk factors in adolescents with type 2 diabetes mellitus—a multicenter study of 578 patients from 225 centres. Pediatr Diabetes 16:204–210. doi:10.1111/pedi.12144
- 33. Huang CJ, Kwok CF, Chou CH, Chou YC, Ho LT, Shih KC (2015) The effect of exercise on lipid profiles and inflammatory markers in lean male adolescents: a prospective interventional study. J Investig Med Off Publ Am Fed Clin Res 63:29–34. doi:10.1097/JIM.00000000000120
- 34. Karoline de Morais P, Sales MM, Alves de Almeida J, Motta-Santos D, Victor de Sousa C, Simões HG (2015) Effects of aerobic exercise intensity on 24-h ambulatory blood pressure in individuals with type 2 diabetes and prehypertension. J Phys Ther Sci 27:51–56. doi:10.1589/jpts.27.51

- Rejeski WJ, Ip EH, Bertoni AG et al (2012) Lifestyle change and mobility in obese adults with type 2 diabetes. N Engl J Med 366:1209–1217. doi:10.1056/NEJMoa1110294
- Schreuder TH, Maessen MF, Tack CJ, Thijssen DH, Hopman MT (2014) Life-long physical activity restores metabolic and cardiovascular function in type 2 diabetes. Eur J Appl Physiol 114:619–627. doi:10.1007/s00421-013-2794-5
- 37. Zhao G, Ford ES, Li C, Mokdad AH (2008) Compliance with physical activity recommendations in US adults with diabetes. Diabet Med J Br Diabet Assoc 25:221–227. doi:10.1111/j.1464-5491.2007.02332.x
- Awodele O, Osuolale JA (2015) Medication adherence in type 2 diabetes patients: study of patients in Alimosho General Hospital, Igando, Lagos, Nigeria. Afr Health Sci 15:513–522. doi:10.4314/ ahs.v15i2.26
- Bagonza J, Rutebemberwa E, Bazeyo W (2015) Adherence to anti diabetic medication among patients with diabetes in eastern Uganda; a cross sectional study. BMC Health Serv Res 15:168. doi:10.1186/s12913-015-0820-5
- 40. Davies MJ, Gagliardino JJ, Gray LJ, Khunti K, Mohan V, Hughes R (2013) Real-world factors affecting adherence to insulin therapy in patients with type 1 or type 2 diabetes mellitus: a systematic review. Diabetic medicine: a journal of the British Diabetic Association 30:512–524. doi:10.1111/dme.12128
- Cochrane J, Chen H, Conigrave KM, Hao W (2003) Alcohol use in China. Alcohol Alcohol 38:537–542. doi:10.1093/alcalc/ agg111
- Hitchman SC, Fong GT (2011) Gender empowerment and female-to-male smoking prevalence ratios. Bull World Health Organ 89:195–202. doi:10.2471/BLT.10.079905
- Fida HR, Abdelmoneim I (2013) Prevalence of smoking among male secondary school students in Jeddah, Saudi Arabia. J Fam Community Med 20:168–172. doi:10.4103/2230-8229.121993
- 44. Masood S, Cappelli C, Li Y et al (2015) Cigarette smoking is associated with unhealthy patterns of food consumption, physical activity, sleep impairment, and alcohol drinking in Chinese male adults. Int J Public Health 60:891–899. doi:10.1007/s00038-015-0730-7