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China Kadoorie Biobank (CKB) Collaborative Group

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SPECIAL FOCUS ISSUE: CARDIOVASCULAR HEALTH PROMOTION

Adherence to Healthy Lifestyle and Cardiovascular Diseases in the Chinese Population



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on behalf of the China Kadoorie Biobank Collaborative Group

ABSTRACT

BACKGROUND Adherence to a combination of healthy lifestyle factors has been related to a considerable reduction of cardiovascular risk in white populations; however, little is known whether such associations persist in nonwhite populations like the Asian population.

OBJECTIVES This study aimed to examine the associations of a combination of modifiable, healthy lifestyle factors with the risks of ischemic cardiovascular diseases and estimate the proportion of diseases that could potentially be prevented by adherence to these healthy lifestyle patterns.

METHODS This study examined the associations of 6 lifestyle factors with ischemic heart disease and ischemic stroke (IS) in the China Kadoorie Biobank of 461,211 participants 30 to 79 years of age who did not have cardiovascular diseases, cancer, or diabetes at baseline. Low-risk lifestyle factors were defined as nonsmoking status or having stopped smoking for reasons other than illness, alcohol consumption of <30 g/day, a median or higher level of physical activity, a diet rich in vegetables and fruits and limited in red meat, a body mass index of 18.5 to 23.9 kg/m², and a waist-to-hip ratio <0.90 for men and <0.85 for women.

RESULTS During a median of 7.2 years (3.3 million person-years) of follow-up, this study documented 3,331 incident major coronary events (MCE) and 19,348 incident ISs. In multivariable-adjusted analyses, current nonsmoking status, light to moderate alcohol consumption, high physical activity, a diet rich in vegetables and fruits and limited in red meat, and low adiposity were independently associated with reduced risks of MCE and IS. Compared with participants without any low-risk factors, the hazard ratio for participants with ≥ 4 low-risk factors was 0.42 (95% confidence interval: 0.34 to 0.52) for MCE and 0.61 (95% confidence interval: 0.56 to 0.66) for IS. Approximately 67.9% (95% confidence interval: 46.5% to 81.9%) of the MCE and 39.1% (95% confidence interval: 26.4% to 50.4%) of the IS cases were attributable to poor adherence to healthy lifestyle.

CONCLUSIONS Adherence to healthy lifestyle may substantially lower the burden of cardiovascular diseases in Chinese. (J Am Coll Cardiol 2017;69:1116-25) © 2017 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).



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Ischemic heart disease (IHD) and ischemic stroke (IS) are posing major burdens to global health (1), and they are the leading causes of death in China (2). Although pharmacological treatment has shown considerable effectiveness in improving therapy of these diseases, it is costly and may have side effects. In contrast, adherence to a healthy lifestyle has become a mainstream approach to lower cardiovascular burden through primary prevention (3).

In epidemiological studies, modifiable lifestyle factors, such as nonsmoking (4), moderate alcohol consumption (5), physical activity (6), healthy diets (7,8), and low adiposity (9,10), have been consistently linked to a reduced cardiovascular risk. Several previous studies showed that adherence to a healthy lifestyle defined by a combination of these modifiable factors was related to up to roughly an 80% reduction in coronary heart disease (CHD) incidence (11-14), and a 50% reduction in IS incidence (15), in white populations from developed countries. However, little is known whether such protective effects persist in other nonwhite populations like the Asian population.

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We thus aimed to examine the associations of a combination of modifiable, healthy lifestyle factors with the risks of IHD and IS in a large cohort of 0.5 million of adult Chinese: the China Kadoorie Biobank (CKB) study (16). In addition, we estimated the proportion of ischemic cardiovascular diseases (CVDs) that could potentially be prevented by adherence to the healthy lifestyle patterns.

METHODS

STUDY POPULATION. The CKB cohort was established in 10 study areas geographically spread across China during 2004 to 2008, when all nondisabled, permanent residents of each area who were 35 to 74 years of age were invited to participate in the study. Of the total of approximately 1.8 million eligible adults in these areas, almost 1 in 3 (33% in rural areas

and 27% in urban areas) responded (17). Overall, 512,891 adults 30 to 79 years of age were enrolled in the study, including a few who were just outside the targeted age range. All participants had completed a questionnaire, had physical measurements taken, and had completed a written informed consent form. The Ethical Review Committee of the Chinese Center for Disease Control and Prevention (Beijing, China) and the Oxford Tropical Research Ethics Committee at the University of Oxford (Oxford, United Kingdom) approved the study. Further details of the CKB cohort have been described in previous publications (16,17).

In the present analysis, we excluded participants who reported previous medical histories of heart disease ($n = 15,472$), stroke ($n = 8,884$), or cancer ($n = 2,577$); had prevalent diabetes ($n = 30,300$) on the basis of self-reported or glucose testing at baseline; had missing data for body mass index (BMI; $n = 2$); or were lost to follow-up shortly after baseline assessment ($n = 3$). After these exclusions, a total of 461,211 participants remained for the current analysis.

ASSESSMENT OF LIFESTYLE FACTORS. Participants reported on a range of lifestyle factors in the baseline questionnaire. Questions about tobacco smoking included frequency, type, and amount of tobacco smoked per day for ever smokers, and years since quitting and the reason for quitting for former smokers. Questions about alcohol consumption included typical drinking frequency, type of alcoholic beverage consumed habitually, and volume of alcohol consumed on a typical drinking day in the past 12 months. Questions about physical activity included the usual type and duration of activities in occupational, commuting, domestic, and leisure time-related domains in the past 12 months. The daily level of physical activity was calculated by multiplying the metabolic equivalent task value for a particular type of activity by hours spent on that activity per day and summing the metabolic equivalent task-hours for all activities. A short qualitative food frequency

ABBREVIATIONS AND ACRONYMS

BMI = body mass index
CHD = coronary heart disease
CKB = China Kadoorie Biobank
CVD = cardiovascular disease
IHD = ischemic heart disease
IS = ischemic stroke
MCE = major coronary events
WHR = waist-to-hip ratio

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questionnaire was used to assess the habitual intakes of 12 conventional food groups in the past 12 months (Online Appendix).

In a subsample of 1,300 participants who completed the same questionnaire twice at an interval of <1.5 years (median 1.4 years), we observed moderate to excellent reproducibility for most of the lifestyle variables. The weighted kappa coefficient was 0.83 for tobacco smoking, 0.66 for alcohol consumption, 0.10 for vegetable intake, 0.40 for fruit intake, and 0.42 for meat intake. The Spearman correlation coefficient was 0.60 for physical activity level. Seasonal availability of fresh vegetables may result in poor reproducibility (18).

Trained staff members measured weight, height, and circumference of waist and hip by using calibrated instruments. BMI was calculated as weight in kilograms divided by height in meters squared. The waist-to-hip ratio (WHR) was the ratio of waist circumference to hip circumference.

ASSESSMENT OF COVARIATES. Covariate information was inquired by baseline questionnaire including sociodemographic characteristics, personal and family medical history, and women's reproductive information. Trained staff members measured blood pressure at least twice by using a UA-779 digital monitor, with the mean of 2 satisfactory measurements used for analyses. A participant was considered as having a family history of a particular disease if he or she reported at least 1 first-degree relative with that disease. Prevalent hypertension was defined as measured systolic blood pressure ≥ 140 mm Hg, measured diastolic blood pressure ≥ 90 mm Hg, a self-reported diagnosis of hypertension, or self-reported use of antihypertensive medication at baseline.

DEFINITION OF LOW-RISK LIFESTYLE. Six dietary and lifestyle factors were considered to define a low-risk lifestyle, namely, smoking, alcohol consumption, physical activity, diet, BMI, and WHR, according to previous studies (11-15,19). For smoking, the low-risk group was defined as nonsmokers or those who had stopped smoking for reasons other than illness for ≥ 6 months. In the CKB cohort, approximately one-half of former smokers quit because of illness (20). We included former smokers who stopped smoking for illness in the current smoker category to avoid a misleadingly elevated risk. For alcohol consumption, the low-risk group was defined as those who drank >0 but <30 g alcohol per day. For physical activity, the low-risk group was defined as those who engaged in a sex-specific median or higher level of physical activity.

For diet, we included 3 food items that are particularly addressed in a 2013 guideline from the

American Heart Association and the American College of Cardiology on lifestyle management to reduce cardiovascular risk (21). The low-risk group was defined as those who ate vegetables and fruits every day and red meat 1 to 6 days a week, consistent with the current recommendation that emphasizes intakes of vegetables and fruits and limits intake of red meats. For general adiposity measured by BMI, the low-risk group was defined as those who had a BMI of 18.5 to 23.9 kg/m², the standard classification of normal weight specific for Chinese (22). For central adiposity measured by WHR, the low-risk group was defined as those who had a WHR <0.90 in men and <0.85 in women (23). Adiposity measures were used to assess energy balance, a critical aspect of a cardiovascular-healthy diet (24).

ASCERTAINMENT OF OUTCOMES. Incident outcome cases since the participants' enrollment into the study at baseline were identified by using linkage with local disease and death registries, with the recently established national health insurance system, and by active follow-up (16). The 10th revision of the International Classification of Diseases (ICD-10) was used to code all cases by trained staff "blinded" to baseline information. The primary outcomes were incident major coronary events (MCE, including IHD [codes I20 to I25] death and nonfatal myocardial infarction [I21 to I23]) and IS [I63]. We also used a broader IHD outcome, which included incident fatal and nonfatal IHD [I20 to I25], in the analysis.

The outcome adjudication process of incident IHD and IS cases has been in place since its inception in 2014. The medical records of cases were retrieved, and the diagnosis was adjudicated centrally by qualified cardiovascular specialists blinded to study assay. By August 2015, of 12,923 incident IHD cases and 13,744 incident IS cases reported since baseline and from patients whose medical records have been retrieved, the diagnosis was confirmed in 82.4% of IHD cases and in 91.8% of IS cases.

STATISTICAL ANALYSIS. Person-years at risk were calculated from the baseline date to the diagnosis of outcomes, death, loss to follow-up, or December 31, 2013, whichever came first. Loss to follow-up in the CKB study referred to a participant who had moved his or her permanent registered residence out of the study area, who could not be contacted after at least 3 times reasonable efforts within 1 year, or who could be contacted but whose new residence was out of the jurisdiction of the Regional Coordinating Center. By December 31, 2013, 2,411 (0.5%) participants were lost to follow-up. The Cox proportional hazards model was used to estimate the hazard ratio (HR) and 95%

TABLE 1 Multivariable-Adjusted HRs (95% CIs) for Incident Ischemic Heart Disease by Lifestyle Factors Among 461,211 Participants

	Major Coronary Events (n _{case} = 3,331)				Ischemic Heart Disease (n _{case} = 21,857)			
	Cases	Cases/PYs (/1,000)	HR (95% CI)	P _{trend} *	Cases	Cases/PYs (/1,000)	HR (95% CI)	P _{trend} *
Smoking								
Never	1,669	0.74	1.00	—	14,060	6.35	1.00	—
Former	154	1.66	1.21 (1.01-1.44)	—	855	9.46	1.09 (1.01-1.18)	—
Current (cigarettes/day)								
<15	670	1.90	1.55 (1.39-1.74)	0.017	2,970	8.57	1.23 (1.18-1.30)	<0.001
15-24	598	1.35	1.69 (1.49-1.91)		2,850	6.55	1.30 (1.23-1.37)	
≥25	240	1.39	1.90 (1.62-2.23)		1,122	6.60	1.43 (1.34-1.54)	
Alcohol consumption								
Never	2,585	0.96	1.00	—	17,706	6.69	1.00	—
Former	249	2.12	1.14 (0.99-1.31)	—	1,168	10.21	1.18 (1.11-1.25)	—
Current weekly	171	0.86	0.86 (0.73-1.01)	—	1,201	6.11	0.91 (0.85-0.97)	—
Current daily (g/day)								
<15	19	1.19	0.57 (0.36-0.90)	0.011	139	8.94	0.79 (0.66-0.93)	0.211
15-29	61	1.05	0.64 (0.50-0.83)		392	6.88	0.78 (0.70-0.86)	
30-59	111	1.12	0.80 (0.66-0.98)		603	6.18	0.80 (0.74-0.87)	
≥60	135	1.03	0.97 (0.81-1.17)		648	4.99	0.83 (0.77-0.91)	
Physical activity (MET-h/day)								
<11.0	1,708	2.13	1.00	<0.001	8,671	11.13	1.00	<0.001
Men 11.0-19.9, Women 11.0-17.9	840	0.98	0.81 (0.75-0.89)		6,198	7.36	0.94 (0.91-0.97)	
Men 20.0-33.4, Women 18.0-29.4	474	0.57	0.69 (0.61-0.77)		4,024	4.92	0.90 (0.86-0.94)	
Men ≥33.5, Women ≥29.5	309	0.37	0.67 (0.58-0.76)		2,964	3.62	0.85 (0.81-0.89)	
Dietary pattern								
Daily FV, weekly but not daily meat	163	0.75	1.00	—	1,717	8.11	1.00	—
Less than daily FV, daily meat	14	0.92	0.99 (0.57-1.73)	—	96	6.39	1.20 (0.97-1.47)	—
Intermediate pattern	3,154	1.02	1.18 (1.00-1.39)	—	20,044	6.61	1.07 (1.01-1.13)	—
BMI (kg/m²)								
<18.5	284	1.97	1.43 (1.26-1.64)	0.054	1,203	8.50	1.16 (1.09-1.23)	<0.001
18.5-23.9	1,642	0.93	1.00		10,010	5.73	1.00	
24.0-27.9	1,039	0.97	1.00 (0.92-1.09)		7,547	7.15	1.10 (1.06-1.14)	
≥28.0	366	1.13	1.03 (0.91-1.18)		3,097	9.82	1.28 (1.22-1.34)	
WHR								
Men <0.90, women <0.85	1,213	0.84	1.00	<0.001	8,248	5.78	1.00	<0.001
Men 0.90-0.94, women 0.85-0.89	915	0.98	1.13 (1.03-1.24)		5,983	6.52	1.05 (1.01-1.09)	
Men ≥0.95, women ≥0.90	1,203	1.29	1.28 (1.16-1.41)		7,626	8.36	1.15 (1.11-1.20)	

Values are cases, cases/PYs, HR, and 95% CI. Multivariable model was adjusted for age, sex, education, marital status, family history of heart attack, and prevalent hypertension at baseline. All 6 lifestyle factors were included simultaneously in the same model. *The linear trend test for smoking was performed only in current smokers, and the linear trend test for alcohol consumption was performed only in current daily drinkers.

BMI = body mass index; CI = confidence interval; FV = fruits and vegetables; HR = hazard ratio; MET = metabolic equivalent task; PY = person-year; WHR = waist-to-hip ratio.

confidence interval (CI), with age as the underlying time scale, and stratified jointly by study area and age at baseline in 5-year intervals.

In the analysis of individual lifestyle factors, the models included all the lifestyle factors simultaneously, as well as age, sex, education, marital status, family histories of heart attack or stroke (adjusted for only in corresponding analysis), prevalent hypertension at baseline, and menopausal status (for women only). The same adjustment was made in the analysis of combined lifestyle factors. The linear trend test for individual factors was performed by assigning the sex-specific median to each category and then modeling this as a continuous variable in a separate model; for

combined lifestyle factors, the test was performed by treating the number of low-risk factors as a continuous variable. The test for interaction with sex or residence was performed by using the likelihood ratio test comparing models with and without a cross-product term.

We calculated population-attributable risk percent (PAR%) (25), an estimate of the percentage of incident cases in this population during follow-up that would not have occurred if all participants had been in the low-risk group, assuming a causal relation. In these analyses, we used a single binary variable and compared participants in the low-risk group for each factor with all other participants, following a method

TABLE 2 Multivariable-Adjusted HRs (95% CIs) for Incident Ischemic Stroke by Lifestyle Factors Among 461,211 Participants

(n _{case} = 19,348)	Cases	Cases/PYs (/1,000)	HR (95% CI)	P _{trend} *
Smoking				
Never	12,141	5.46	1.00	—
Former	839	9.28	0.98 (0.91-1.06)	—
Current (cigarettes/day)				
<15	2,756	7.95	1.17 (1.11-1.23)	0.018
15-24	2,655	6.09	1.22 (1.16-1.29)	
≥25	957	5.62	1.22 (1.13-1.31)	
Alcohol consumption				
Never	15,230	5.73	1.00	—
Former	1,111	9.70	1.24 (1.16-1.32)	—
Current weekly	1,079	5.47	0.90 (0.84-0.96)	—
Current daily (g/day)				
<15	170	10.96	0.94 (0.81-1.10)	0.029
15-29	422	7.40	0.90 (0.81-0.99)	
30-59	680	6.97	1.00 (0.92-1.09)	
≥60	656	5.06	1.06 (0.97-1.15)	
Physical activity (MET-h/day)				
<11.0	8,713	11.18	1.00	<0.001
Men 11.0-19.9, Women 11.0-17.9	5,482	6.49	0.92 (0.89-0.96)	
Men 20.0-33.4, Women 18.0-29.4	2,994	3.65	0.89 (0.85-0.93)	
Men ≥33.5, Women ≥29.5	2,159	2.63	0.84 (0.79-0.88)	
Dietary pattern				
Daily FV, weekly but not daily meat	1,397	6.56	1.00	—
Less than daily FV, daily meat	133	8.87	1.35 (1.12-1.61)	—
Intermediate pattern	17,818	5.86	1.13 (1.07-1.20)	—
BMI (kg/m²)				
<18.5	786	5.52	0.94 (0.88-1.02)	<0.001
18.5-23.9	8,756	5.00	1.00	
24.0-27.9	7,136	6.75	1.09 (1.05-1.13)	
≥28.0	2,670	8.42	1.14 (1.09-1.20)	
WHR				
Men <0.90, women <0.85	6,712	4.68	1.00	<0.001
Men 0.90-0.94, women 0.85-0.89	5,690	6.19	1.12 (1.08-1.16)	
Men ≥0.95, women ≥0.90	6,946	7.60	1.15 (1.11-1.20)	

Values are cases, cases/PYs, HR, and 95% CI. Multivariable model was adjusted for age, sex, education, marital status, family history of stroke, and prevalent hypertension at baseline. All 6 lifestyle factors were included simultaneously in the same model. *The linear trend test for smoking was performed only in current smokers, and the linear trend test for alcohol consumption was performed only in current daily drinkers.

Abbreviations as in Table 1.

RESULTS

The mean age of the participants was 50.7 ± 10.5 years. Of 461,211 participants, 1.0%, 13.7%, and 41.3% had at least 5, 4, and 3 low-risk lifestyle factors, respectively. Participants who were women, younger, more educated, and urban residents were more likely to adhere to a healthy lifestyle (Online Table 1).

During a median of 7.2 years (3.3 million person-years) of follow-up, we documented 3,331 incident MCE (including 2,179 IHD deaths and 1,152 nonfatal myocardial infarctions), 21,857 IHD cases, and 19,348 IS cases. All lifestyle factors were associated with the risks of MCE, IHD, and IS (Tables 1 and 2, Online Table 2). Multivariable-adjusted analysis showed that smoking, being underweight, and central adiposity were associated with increased risk of MCE; light to moderate alcohol consumption, high physical activity, and a diet rich in vegetables and fruits and limited in red meat were associated with a reduced risk of MCE. For most of the lifestyle factors, similar associations, but smaller in magnitude, were observed with IHD and IS. Different from MCE, overweight status and obesity defined by BMI were associated with increased risks of IHD and IS, and underweight status was also related to an increased risk of IHD. All associations of lifestyle factors with the risks of incident MCE, IHD, and IS were consistently observed in both men and women (p > 0.05 for interaction with sex), except for the associations of MCE with smoking (p_{interaction} = 0.002) and dietary pattern (p_{interaction} = 0.010) and the association of IS with WHR (p_{interaction} = 0.030) (Online Tables 3 and 4).

When the 6 lifestyle factors were collapsed into binary categories, all the low-risk groups were associated with reduced risks of MCE, IHD, and IS (Table 3, Online Table 5); most of these associations were consistently observed between men and women (Online Table 6) and between urban and rural residents (Online Table 7). The risks of MCE, IHD, and IS decreased significantly with an increasing number of any low-risk factors in the whole cohort (Figure 1, Online Table 8) and in both men and women (Online Table 9) (all p for linear trend <0.001). Compared with participants who were not in the low-risk group of any factors, the adjusted HRs of participants who had 4 or more low-risk factors was 0.42 (95% CI: 0.34 to 0.52) for MCE, 0.57 (95% CI: 0.53 to 0.61) for IHD, and 0.61 (95% CI: 0.56 to 0.66) for IS.

To test the robustness of the findings, we examined potential confounding of socioeconomic status

previously suggested by Wacholder et al. (26). We further estimated the PAR% according to sex, residence, age, family histories of heart attack or stroke, and the presence of hypertension; and we repeated the analysis among never-regular smokers, never-regular drinkers, participants who were not underweight, and diabetic participants at baseline.

The statistical analyses were performed using Stata (version 13.1, StataCorp, College Station, Texas). The calculation of PAR% was performed using SAS (version 9.4, SAS Institute, Cary, North Carolina). All p values were 2-sided, and statistical significance was defined as p < 0.05.

by adding occupation and household income to the model, or including participants who had diabetes at baseline in the analysis and adjusting for diabetes in the model, or adjusting for systolic blood pressure and the use of cardiovascular medications. To minimize potential bias resulting from subclinical conditions, we performed analyses by further excluding participants whose cardiovascular outcomes occurred in the first 2 years of follow-up or excluding underweight participants (BMI <18.5 kg/m²). These sensitivity analyses did not substantially alter the risk estimates (data not shown).

Table 3 (and **Online Tables 6 and 7**) presents the PAR% for each lifestyle factor. The combined PAR% of MCE in relation to smoking, lack of physical activity, and unhealthy diet was 44.8% (95% CI: 26.3% to 60.2%), which increased to 51.4% (95% CI: 32.0% to 66.7%) when additionally considering general and central adiposity (**Central Illustration, Online Table 10**). The PAR% for all 6 factors was 67.9% (95% CI: 46.5% to 81.9%) for MCE, a finding suggesting that approximately two-thirds of the incident MCE in this population during follow-up period might have been prevented if all participants had been in the low-risk group for 6 factors. The risk attributable to these modifiable lifestyle factors was lower for IHD and IS. The PAR% for 6 factors was 43.2% (95% CI: 32.1% to 53.1%) for IHD and 39.1% (95% CI: 26.4% to 50.4%) for IS.

The PAR% estimates appeared to be similar for men and women, for urban and rural residents, for different age groups, for participants with or without a family history of heart attack or stroke, and for participants with or without hypertension (**Online Table 10**). The potential reductions in risks of MCE, IHD, and IS among never-regular smokers or never-regular drinkers, although with wider CIs, were generally consistent with those observed in the whole study population (**Online Table 11**). Exclusion of underweight participants from the analysis did not substantially alter the PAR% estimates. When we estimated the PAR% in the participants with diabetes at baseline who were excluded from the primary analysis, a larger reduction in risk of IHD was observed in relation to smoking, physical activity, dietary pattern, and adiposity.

DISCUSSION

In this large, prospective cohort of 0.5 million middle-aged to older Chinese, adhering to a healthy lifestyle (i.e., never smoking or stopping smoking not for illness, consuming alcohol lightly or moderately, being physically active, eating a diet rich in vegetables

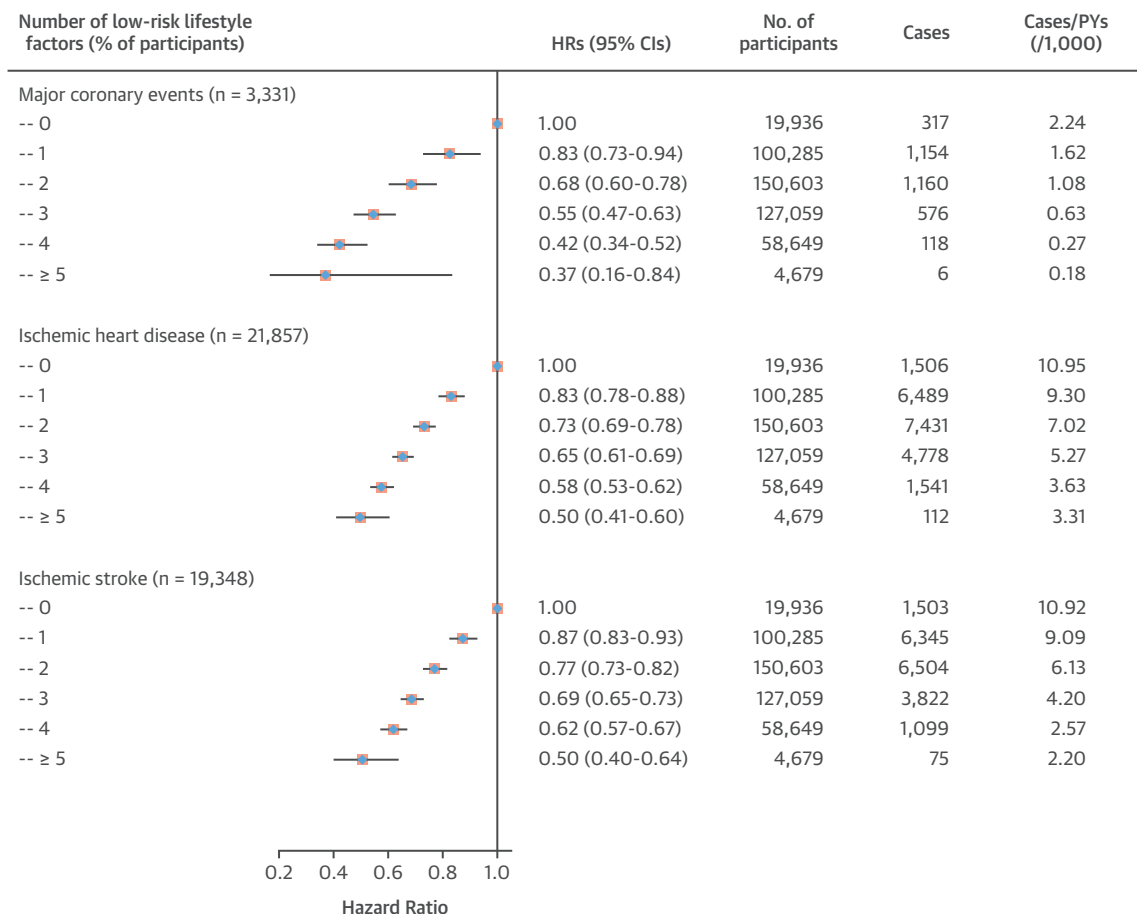
TABLE 3 Multivariable-Adjusted HRs (95% CIs) and PAR% (95% CIs) for Incident Ischemic CVDs by Low-Risk Lifestyle Factors* Among 461,211 Participants

	Cases in Low-Risk Group	Cases/PYs (1,000) in Low-Risk Group	HR (95% CI)	PAR% (95% CI)
Major coronary events (n_{case} = 3,331)				
Smoking	1,823	0.78	0.63 (0.57-0.69)	16.9 (14.5-19.2)
Alcohol consumption	80	1.08	0.64 (0.51-0.80)	33.9 (18.7-47.5)
Physical activity	783	0.47	0.74 (0.68-0.82)	21.6 (15.9-27.1)
Dietary pattern	163	0.75	0.84 (0.72-0.99)	15.2 (1.7-28.1)
BMI	1,642	0.93	0.89 (0.83-0.95)	5.8 (2.1-9.4)
WHR	1,213	0.84	0.89 (0.83-0.96)	6.4 (1.8-11.0)
Ischemic heart disease (n_{case} = 21,857)				
Smoking	14,915	6.47	0.80 (0.77-0.83)	6.5 (5.5-7.5)
Alcohol consumption	531	7.32	0.80 (0.73-0.87)	19.5 (12.4-26.3)
Physical activity	6,988	4.27	0.90 (0.87-0.93)	8.0 (5.8-10.1)
Dietary pattern	1,717	8.11	0.94 (0.89-0.99)	6.2 (1.6-10.7)
BMI	10,010	5.73	0.86 (0.84-0.89)	7.8 (6.2-9.3)
WHR	8,248	5.78	0.91 (0.88-0.94)	5.2 (3.5-7.0)
Ischemic stroke (n_{case} = 19,348)				
Smoking	12,980	5.61	0.83 (0.80-0.87)	5.5 (4.4-6.6)
Alcohol consumption	592	8.16	0.90 (0.82-0.97)	8.6 (1.1-16.1)
Physical activity	5,153	3.14	0.90 (0.87-0.93)	9.2 (6.7-11.7)
Dietary pattern	1,397	6.56	0.89 (0.84-0.94)	10.8 (6.0-15.6)
BMI	8,756	5.00	0.92 (0.89-0.95)	4.5 (2.8-6.1)
WHR	6,712	4.68	0.86 (0.83-0.89)	8.8 (6.8-10.7)

Values are cases, cases/PYs, HR, PAR%, and 95% CI. The multivariable model was adjusted for age, sex, education, marital status, family histories of heart attack or stroke (adjusted for in the corresponding analysis), and prevalent hypertension at baseline. All 6 lifestyle factors were included simultaneously in the same model. *Low-risk lifestyle factors were defined as follows: nonsmoking status or having stopped smoking for reasons other than illness; drinking >0 but <30 g of alcohol per day; engaging in a sex-specific median or higher level of physical activity; eating fruits and vegetables every day and red meat 1 to 6 days a week; having a BMI between 18.5 and 23.9 kg/m²; and having a WHR <0.90 in men and <0.85 in women.
CVD = cardiovascular disease; PAR% = population-attributable risk percent; other abbreviations as in **Table 1**.

and fruits and limited in red meat, and maintaining a normal BMI and a lower WHR) was associated with a significantly reduced risk of ischemic CVDs. Compared with participants without any of the low-risk lifestyle factors, participants who had at least 4 low-risk factors showed a 58%, 43%, and 39% reduction in relative risk of MCE, IHD, and IS, respectively. If observed associations are causal, two-thirds of MCE, two-fifths of IHD cases, and two-fifths of IS cases in this population during a median 7.2 years of follow-up could have been avoided by adherence to a healthy lifestyle.

Our findings are consistent with previous cohort studies conducted in the U.S. (11,14,15,19) and European populations (12,13,27), thus indicating that the reduction in relative risk of CVD incidence or death is proportional to the increased number of healthy lifestyle factors. Findings from the Nurses' Health Study of 15- to 20-year follow-up data showed that the PAR% for the combination of smoking, alcohol consumption, physical activity, diet, and BMI was 82% (95% CI: 58% to 93%) for CHD

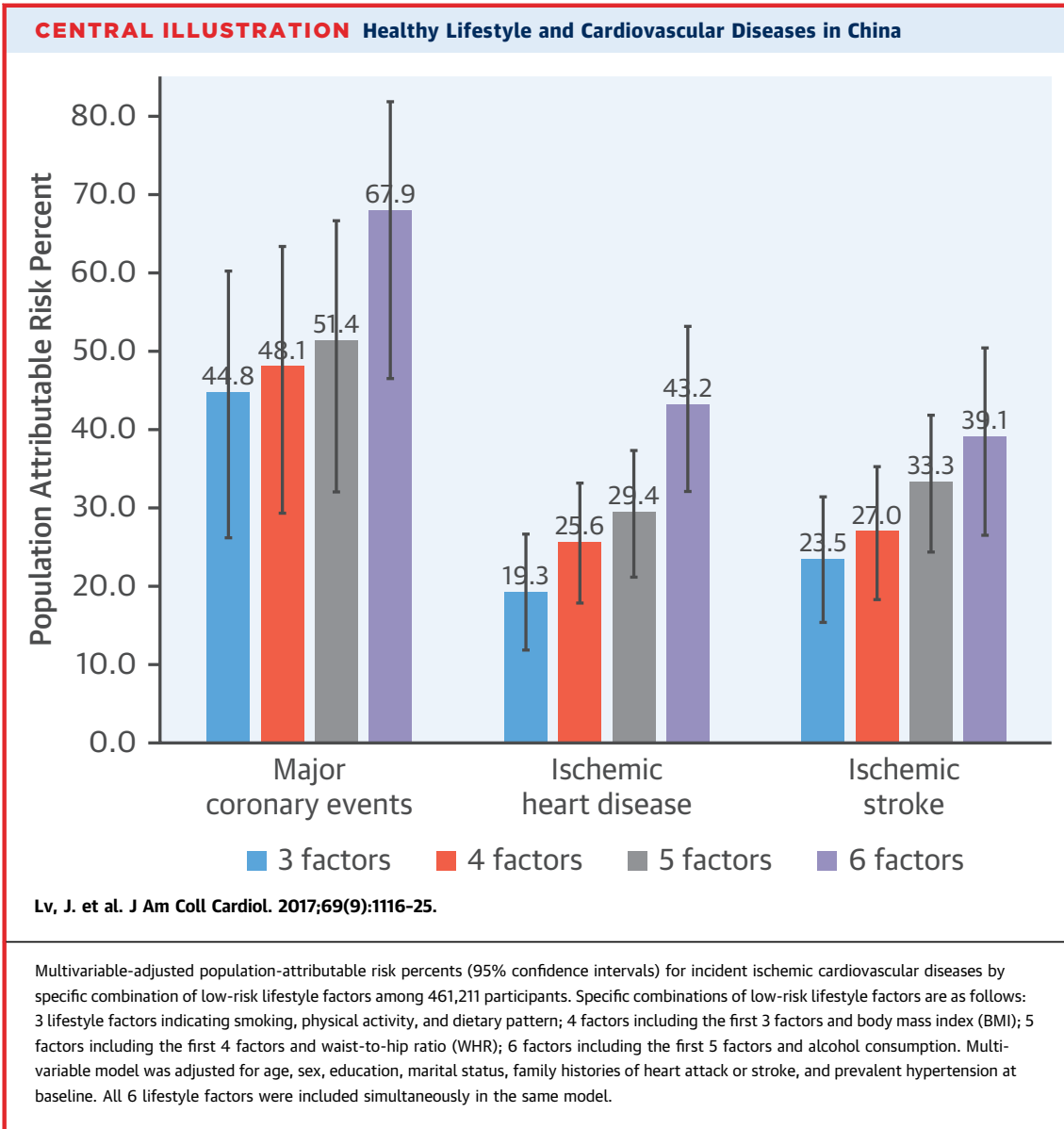
FIGURE 1 Multivariable-Adjusted HRs (95% CIs) for Incident Ischemic Cardiovascular Diseases by Number of Low-Risk Lifestyle Factors Among 461,211 Participants

Horizontal lines represent the 95% confidence interval (CI). This multivariable model was adjusted for age, sex, education, marital status, family histories of heart attack or stroke, and prevalent hypertension at baseline. The hazard ratios (HRs) for the number of low-risk lifestyle factors were calculated by creating indicator variables. PY = person-year.

incidence (11), 54% (95% CI: 15% to 78%) for IS incidence (15), and 74% (95% CI: 55% to 86%) for CVD incidence (11). Similar PARs% were estimated in other findings from the U.S. and Swedish cohorts (12-15). A further analysis of 24-year follow-up data of the Nurses' Health Study showed that 75.2% (95% CI: 60.9% to 84.7%) of CVD deaths could be attributed to the foregoing 5 factors (19). In a study conducted in older Europeans, 70 to 90 years of age, lack of adherence to the low-risk pattern of smoking, alcohol consumption, physical activity, and diet was associated with a 64% increase of CHD death and a 61% increase of CVD death during a 10-year period (27). The longer duration of follow-up and a population characterized by higher education and socio-economic status may partly explain the observed

higher PAR% for CVDs in the U.S. cohorts than those observed in our Chinese population.

A prospective study from the Shanghai Women's Health Study quantified the combined impact of a healthier lifestyle pattern, including normal BMI, lower WHR, participation in physical exercise, lack of exposure to spousal smoking, and higher fruit and vegetable intake, on CVD death in lifetime nonsmoking and nondrinking Chinese women 40 to 70 years of age (28). The PAR% for having 4 to 5 unhealthy lifestyle factors was 58.7% for CVD death during 9-year follow-up. However, this study included only women from 1 of the most developed cities of China, and the small number of incident cases precluded further analyses on different types of CVDs. The present study comprehensively assessed the relationship between a



combination of multiple lifestyle factors and various CVD outcomes in Chinese.

In the present study, we observed that the PAR% was higher for IHD than for IS, a finding consistent with observations reported in the Nurses' Health Study (11,15). A possible explanation is that IS has risk factors that partly differ from those of IHD.

Light to moderate alcohol consumption was shown to have a particularly important protective effect on IHD in our population. Nevertheless, even light to moderate drinking may increase the risk of other outcomes such as cancer (29,30). Therefore, we would be cautious about recommending alcohol consumption for overall human health (31,32). In the present population, one-half of MCE and one-third of IS cases

might have been prevented by compliance with the remaining components of the low-risk lifestyle irrespective of alcohol consumption.

This large, prospective study quantified the burden of ischemic CVDs that could be prevented through adherence to a set of well-studied modifiable lifestyle factors. The large number of incident cases provides reliable estimates. Our study provided evidence for the joint beneficial effects of multiple lifestyle factors on prevention of ischemic CVDs in the nationally representative general Chinese population. The inclusion of a geographically spread population living in urban and rural areas, with different sociodemographic characteristics such as sex, education, income, and occupation, makes our results broadly

applicable. We carefully controlled for potential confounding factors and sought to minimize the reverse causation bias by excluding participants with major chronic diseases at baseline that could lead to lifestyle changes. We further excluded participants whose cardiovascular outcomes occurred in the first 2 years of follow-up and underweight participants, to address the concern of subclinical disease; the results remained virtually unchanged. In addition, the anthropometric information was measured rather than self-reported in our cohort, thereby providing more accurate estimates of BMI and WHR.

STUDY LIMITATIONS. The lifestyle behaviors were self-reported, potentially leading to some misclassification. The questionnaire on lifestyle factors used in the CKB study has not yet been validated directly; however, these questions were adapted from validated questionnaires used in several other studies, with some additional modifications after a pilot study. Such measurement errors, however, may be nondifferential on subsequent disease status and tend to attenuate the association. The lifestyle factors were measured once at baseline and may not necessarily reflect long-term patterns. Residual confounding by other unmeasured or unknown factors, particularly socioeconomic status, was still possible. However, adjustment for education, occupation, and household income had little influence on the findings. In addition, the lack of detailed dietary information and quantitative measure of food consumption in this study limited our ability to capture the complexity of the dietary patterns comprehensively. Nevertheless, the limited food items included in our study have shown consistent associations with CVD outcomes of interest, and the guidelines for these foods are also easy to follow. Lack of further classification of IS subtypes may undervalue the role of lifestyle factors in some specific subtypes of IS.

CONCLUSIONS

This large, prospective cohort of Chinese adults provided convincing epidemiological evidence that adherence to a healthy lifestyle (i.e., abstinence from

or cessation of smoking, light to moderate alcohol consumption, consumption of a healthy diet, physically activity, and maintenance of a healthy weight without central adiposity) would prevent approximately two-thirds of MCE and two-fifths of IS over a period of <10 years. A larger reduction in CVD risk can be expected with the addition of other preventable factors. This study provides critical quantitative estimates of the potential effect of a population-based lifestyle intervention on the growing burden of ischemic CVDs in China. Extended follow-up of this cohort would provide further evidence of the longer-term impact of overall lifestyle modification in disease prevention.

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PERSPECTIVES

COMPETENCY IN SYSTEMS-BASED PRACTICE: Adherence to a healthy lifestyle in China is associated with a substantially lower risk of CVD.

TRANSLATIONAL OUTLOOK: Now that the efficacy of adherence to a healthy lifestyle has been validated in this Chinese population, attention should be directed to the development of strategies that encourage broad swaths of the Chinese population to adopt and maintain healthy behaviors.

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- KEY WORDS** cardiovascular diseases, cohort studies, health behavior, lifestyle
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- APPENDIX** For a complete list of the members of the China Kadoorie Biobank Steering Committee and Collaborative Group and a questionnaire as well as supplemental tables, please see the online version of this paper.