Ideal cardiovascular health and mortality: pooled results of three prospective cohorts in Chinese adults

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Abstract

Background: Evidence on the relations of the American Heart Association's ideal cardiovascular health (ICH) with mortality in Asians is sparse, and the interaction between behavioral and medical metrics remained unclear. We aimed to fill the gaps.

Methods: A total of 198,164 participants without cancer and cardiovascular disease (CVD) were included from the China Kadoorie Biobank study (2004–2018), Dongfeng-Tongji cohort (2008–2018), and Kailuan study (2006–2019). Four behaviors (i.e., smoking, physical activity, diet, body mass index) and three medical factors (i.e., blood pressure, blood glucose, and blood lipid) were classified into poor, intermediate, and ideal levels (0, 1, and 2 points), which constituted 8-point behavioral, 6-point medical, and 14-point ICH scores. Results of Cox regression from three cohorts were pooled using random-effects models of meta-analysis.

Results: During about 2 million person-years, 20,176 deaths were recorded. After controlling for demographic characteristics and alcohol drinking, hazard ratios (95% confidence intervals) comparing ICH scores of 10–14 *vs.* 0–6 were 0.52 (0.41–0.67), 0.44 (0.37–0.53), 0.54 (0.45–0.66), and 0.86 (0.64–1.14) for all-cause, CVD, respiratory, and cancer mortality. A higher behavioral or medical score was independently associated with lower all-cause and CVD mortality among the total population and populations with different levels of behavioral or medical health equally, and no interaction was observed.

Conclusions: ICH was associated with lower all-cause, CVD, and respiratory mortality among Chinese adults. Both behavioral and medical health should be improved to prevent premature deaths.

Keywords: China; Health behavior; Ideal cardiovascular health; Metabolic health; Mortality; Noncommunicable diseases; Body mass index; Smoking; Alcohol; Exercise

Introduction

In 2010, the American Heart Association (AHA) proposed the ideal cardiovascular health (ICH), also known as the Life's Simple 7, which is defined by the presence of both ideal health behaviors (including non-smoking, physical activity at recommended levels, body mass index [BMI] of <25.0 kg/m^2, and healthy diets consistent with current guidelines/recommendations) and ideal medical factors (including untreated blood pressure, fasting blood glucose [FBG], and blood total cholesterol [TC] levels of <120/80 mmHg, 5.6 mmol/L, and 5.2 mmol/L, respectively).[1] Those behavioral and metabolic factors are major determinants of the global disease burden, including but not limited to cardiovascular disease (CVD).[2]

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Increasing studies have investigated the association of ICH with mortality. Our recent meta-analysis of 16 studies found that the highest ICH score category was associated with 45% to 61% risk reductions in all-cause and CVD mortality.[3] However, most studies were conducted in high-income and Western countries, and studies in middle- or low-income countries are lacking. This is important considering that socioeconomic factors could be upstream determinants of cardiovascular health, and implementation of health policies varied in different countries.[4] Besides, previous studies have reported the associations of ICH with risks of CVD subtypes, cancer, and respiratory diseases[3,5-7]; however, few studies have investigated associations of ICH with mortality from subtypes of CVD,[8,9] cancer,[7] and respiratory diseases, which are important to the tertiary prevention of major non-communicable diseases.

Moreover, the ICH score included both behavioral and medical factors, while their interaction and independent associations with mortality were seldom investigated, which could clarify the roles of behavioral and medical metrics in mortality and facilitate risk stratification in healthcare.[10] Thus, we investigated associations of ICH with all-cause and cause-specific mortality in three Chinese cohorts, and we investigated the interaction and independent associations of behavioral and medical scores with mortality. Given the different study designs, data collection tools, and population characteristics, all analyses were performed in each cohort first, and the results were then pooled by meta-analysis approach according to previous studies.[11,12]

Methods

Ethics approval

All participants provided their written informed consent. The study was approved by the Ethics Committees of the China National Center for Disease Control and Prevention (Approval No. 005/2004) and the Oxford University (Approval No. 025–04) for the China Kadoorie Biobank (CKB) study, the Dongfeng General Hospital and the Huazhong University of Science and Technology (Approval Nos. 2008–03 and 2012–10) for the Dongfeng-Tongji (DFTJ) cohort, and the Kailuan General Hospital for the Kailuan study (Approval No. 200608).

Study population

This study used three ongoing cohorts in China: the CKB study, DFTJ cohort, and Kailuan study. Briefly, the CKB study recruited 512,891 residents aged 30 to 79 years from ten regions including five rural counties (from Gansu, Henan, Hunan, Sichuan, and Zhejiang provinces) and five urban cities (from Guangxi Zhuang Autonomous Region, Hainan, Heilongjiang, Jiangsu, and Shandong provinces) between 2004 and 2008.[13] Approximately 5% of the participants from the CKB study were resurveyed in 2008 and 2013 to 2014, respectively.[14] The DFTJ cohort is a dynamic cohort consecutively recruiting retirees from the Dongfeng Motor Corporation, Shiyan, Hubei Province, China,[15] which was launched in 2008 and recruited 27,009 participants in 2008 to 2010. The first follow-up was conducted in 2013; meanwhile, 14,120 new retirees were additionally enrolled. The Kailuan study is a dynamic cohort in the Kailuan community in Tangshan, Hebei Province, China.[16] It was launched in 2006 and recruited 101,510 employees aged 18 to 98 years of the Kailuan Group in 2006 to 2007. Subsequent surveys were conducted every two years, and 25,337, 10,519, and 21,651 new participants were additionally recruited in 2008 to 2009, 2010 to 2011, and 2012 to 2013, respectively. Participants were invited to complete questionnaires and medical examinations, and blood was drawn at each survey. Each participant's baseline was set at the first survey when all ICH metrics and covariates were measured.

The DFTJ cohort and Kailuan study planned to measure all participants' blood lipid levels; however, the CKB study only measured blood lipids from 37,287 participants. The current analysis was based on 237,433 participants (37,287 with measured blood lipid markers from the CKB study, 41,129 from the DFTJ cohort, and 159,017 from the Kailuan study). We excluded 17,972 participants (1993, 6147, and 9832, respectively, from the three cohorts) with missing data on ICH metrics and 6834 participants (116 from the DFTJ cohort and 6718 from the Kailuan study) with missing covariates including demographic characteristics and alcohol consumption. Considering that diagnoses and treatments of cancer and CVD could change patients' ICH metrics and their future mortality risks, 14,463 patients with cancer or CVD (1628, 7886, and 4949, respectively, from the three cohorts) were excluded to mitigate reverse causation according to previous studies.[3] The final analysis included 198,164 participants (33,666, 26,980, and 137,518, respectively, from the three cohorts; Supplementary Figure 1, http://links.lww.com/CM9/B171).

Assessment of ICH

We created an ICH score according to the AHA's definition,[1] and some modifications were made to accommodate the methodology of three cohorts [Supplementary Table 1, http://links.lww.com/CM9/B171].

Current status of cigarette smoking and years since quitting smoking were self-reported. The AHA defined quitting smoking for ≥1 year as ideal level; however, a previous study found that only quitting smoking for ≥10 years was consistently associated with lower mortality risks from all causes, total and subtypes of CVD, respiratory disease, and smoking-caused or other cancers compared with current smoking.[17] Besides, two-thirds of individuals who tried to quit smoking relapsed to smoking in China,[18] and the relapse rate keeps increasing before 8 years of quitting smoking.[19] Accordingly, smoking was categorized into ideal, never smoking or quitting smoking for ≥10 years; intermediate, quitting smoking for <10 years; and poor, current smoking.

Weekly time spent on moderate and vigorous activities was obtained in the CKB study, while weekly time spent on walking, bicycling, dancing, Tai chi, gymnasium, balls, jogging, swimming, and climbing were obtained in the

DFTJ cohort. Since most participants from the DFTJ cohort met the recommendation of weekly 150-min moderate-to-vigorous leisure-time physical activity, we divided participants into tertiles according to leisure-time physical activity (ideal, top; intermediate, medium; and poor, bottom) in the DFTJ cohort and CKB study to make the results comparable. In the Kailuan study, one question (i.e., "How often did you exercise in recent 5 years?") with three options (ideal, >80 min/week; intermediate, 1–80 min/week; poor, none) was applied according to a previous study.[16]

Dietary habits were determined via simplified food frequency questionnaires (including rice, wheat, whole grain, red meat, poultry, seafood, egg, fresh vegetable, beans, pickles, fresh fruit, and dairy intakes) in the CKB study and DFTJ cohort. According to a previous study and current recommendations emphasizing increasing vegetable and fruit intakes while limiting red meat intakes,[20] a dietary metric composed of daily consuming vegetable, daily consuming fruit, and not daily consuming red meat was created: ideal, three components; intermediate, two components; poor, 0 to 1 component. According to a previous publication from the Kailuan study,[16] salt intakes obtained by "What's your daily salt intake? ideal, <6 g; intermediate, 6–12 g; poor, >12 g" were used as a surrogate for dietary quality in the Kailuan study since no other dietary information was available. A previous study from Kailuan study (2013–2014) found a strong association between salt intake and a healthy diet score consisting of vegetables, fruits, whole grains, fish, sweets, sugar-sweetened beverages, and sodium (the age- and gender-adjusted mean healthy diet score was 1.87, 0.98, and 0.70 among those with ideal, intermediate, and poor salt intakes, respectively).[21]

Standing height and body weight were measured in participants with light indoor clothing and without shoes. BMI was calculated as weight in kilograms divided by height in meters squared: ideal, 18.5 to 24.9 kg/m^2; intermediate, 25.0 to 29.9 kg/m^2; poor, <18.5 kg/m^2 or ≥30.0 kg/m^2.

Resting blood pressure was measured: ideal, systolic blood pressure (SBP)/diastolic blood pressure (DBP) <120/80 mmHg without self-reported treatment; intermediate, 120–139/80–89 mmHg, or <120/80 mmHg with treatment; poor, ≥140/90 mmHg.

FBG was measured using the Aeroset automatic analyzer (ABBOTT Laboratories, Chicago, IL, USA) in the DFTJ cohort and Hitachi 747 automatic analyzer (Hitachi, Tokyo, Japan) in the Kailuan study. Random blood glucose was measured by rapid dipstick testing using the Johnson SureStep Plus (LifeScan, Milipitas, California, USA) in the CKB study, and FBG would be measured the next day when one's random blood glucose was 7.8 to 11.0 mmol/L. Blood glucose health was categorized into ideal, FBG <5.6 mmol/L or random blood glucose <7.8 mmol/L without self-reported treatment; intermediate, FBG 5.6 to 6.9 mmol/L or random blood glucose 7.8 to 11.0 mmol/L, or FBG <5.6 mmol/L or random blood glucose <7.8 mmol/L with treatment; poor, FBG ≥7.0 mmol/L or random blood glucose ≥11.1 mmol/L.

Blood lipid levels were measured using the AU680 Chemistry Analyzers (Beckman-Coulter, Brea, CA, USA) in the CKB study, ARCHITECTCi8200 automatic analyzer (ABBOTT Laboratories) in the DFTJ cohort, and Hitachi 747 automatic analyzer (Hitachi) in the Kailuan study. Since most studies found no associations between ideal TC and mortality,[10,22-27] we used low-density lipoprotein cholesterol (LDL-C), a better prognostic factor for incidence and prognosis of CVD,[28] to evaluate blood lipid: ideal, LDL-C <3.4 mmol/L without self-reported treatment; intermediate, 3.4 to 4.0 mmol/L, or <3.4 mmol/L with treatment; poor, ≥4.1 mmol/L.[28]

For each metric, 2, 1, or 0 points were assigned for ideal, intermediate, or poor level, and the score ranged between 0 and 14. Based on previous studies,[29,30] ICH score was equally divided into three groups according to the range, that is, scores 0–4, 5–9, and 10–14. However, there were too few individuals with scores 0–4 (1.1% in the CKB study, 1.1% in the DFTJ cohort, and 1.5% in Kailuan study), and participants were regrouped into inadequate (scores 0–6), average (scores 7–9), and optimum (scores 10–14) to increase statistical power, which was also consistent with a previous study.[29] We further used four behavioral metrics (i.e., cigarette smoking, physical activity, diet, and BMI) to construct an 8-point behavioral score and three medical metrics (i.e., blood pressure, blood glucose, and blood lipid levels) to construct a 6-point medical score. To ensure sufficient statistical power for interaction analyses, participants were divided into three groups with roughly similar sample sizes according to the behavioral score (i.e., 0–4, 5–6, and 7–8) and medical score (i.e., 0–3, 4, and 5–6), respectively.

Assessment of covariates

Age, gender, region (only in the CKB study), marital status, education level, income level (the CKB and Kailuan studies), occupation (the CKB study), and alcohol drinking were self-reported. Prevalent hypertension (defined as self-reported physician diagnosis or uses of antihypertensive medications, or SBP ≥140 mmHg or DBP ≥90 mmHg) and prevalent diabetes (defined as self-reported physician diagnosis or uses of anti-diabetic medications, or FBG ≥7.0 mmol/L or random blood glucose ≥11.1 mmol/L) were also considered for stratified analyses.

Assessment of outcomes

In the CKB study, vital status and causes of deaths were determined via official death certificates supplemented with medical records, residential records, active visiting local communities, hospital records, or verbal autopsies through December 31, 2018. The Dongfeng Motor Corporation's healthcare service system covering all retirees was used to determine the mortality status of participants through December 31, 2018. In the Kailuan study, deaths were ascertained through discharge lists from local hospitals, official death certificates, and active follow-ups, through December 31, 2019, while causes of deaths, which need extra time for adjudication by investigators especially during the coronavirus disease 2019 (COVID-19) pandemic, are currently updated to December 31, 2016; thus, the end of follow-up was set as December 31, 2019 for all-cause mortality and December 31, 2016 for cause-specific mortality in the Kailuan study. International Classification of Diseases Tenth Revision (ICD-10) codes were used to identify deaths from cancer (C00-C97), CVD (I00-I99), ischemic heart disease (IHD, I20-I25), stroke (I60, I61, I63, and I64), and respiratory disease (J00-J99).

Statistical analysis

Covariate distributions across baseline ICH scores were compared using the Kruskal–Wallis test for continuous variables and chi-squared test for categorical variables. We also compared covariate distributions between those included in and excluded from the analyses due to missing information in each cohort, and an absolute standardized difference of <0.1 indicated a negligible difference between two groups.[31]

We then used Cox regression models to investigate the associations of ICH score and its components with mortality, the independent associations of behavioral and medical scores with mortality, and the interaction between behavioral score and medical score. We also conducted several subgroup and sensitivity analyses. We controlled for age, gender, region (in the CKB study), marital status, education level, income level (the CKB and Kailuan studies), occupation (the CKB study), and alcohol drinking in all analyses, and these covariates were selected *a priori* according to previous studies.[3] All analyses were first performed within each cohort, and then we pooled hazard ratios (HRs) with confidence intervals (CIs) from three cohorts using random-effects models of meta-analysis according to previous studies[11,12] since the results from three cohorts were largely consistent. We chose random-effects models to allow heterogeneity in different cohorts, including differences in study design, participant characteristics, data collection, and variable definitions. Dose-response meta-analyses were conducted using the Greenland and Longnecker method to test both linear and nonlinear relations between the ICH score and mortality.[32]

Cox regression models were used to investigate the association of the ICH score with all-cause mortality, and competing risks were considered for cause-specific mortality. The ICH score was included in models as continuous and categorical variables, respectively. We also investigated the independent association between each ICH metric and mortality.

To illustrate independent associations of combined behavioral metrics and combined medical metrics, we mutually adjusted for the behavioral and medical scores in models. We further investigated associations between the behavioral score and mortality across participants with different medical scores, and associations between the medical score and mortality across participants with different behavioral scores.

Stratified analyses were conducted by age, gender, education level, alcohol consumption, and prevalent diabetes and hypertension. Meta-regressions were used to estimate *P* values for the difference between subgroups. Several sensitivity analyses were also conducted. First, deaths occurring within the first 3 years of follow-up were excluded to reduce reverse causation. Second, we applied the original AHA's definition of ICH metrics without modification (except for diet in three cohorts and physical activity in the Kailuan study; Supplementary Table 1, http://links.lww.com/CM9/B171). Third, we additionally excluded individuals with prevalent emphysema or chronic bronchitis at baseline given that respiratory disease could change patients' smoking habits. However, the Kailuan study did not collect the information on respiratory disease history, so we excluded no participants from the Kailuan study in this sensitivity analysis. Fourth, we additionally adjusted for family history of diabetes, CVD, and cancer to account for the genetic background. Fifth, to eliminate the impact of non-responses, we performed the multiple imputation with five imputed datasets to impute missing covariates according to non-missing variables. Sixth, a 7-point ICH score was constructed by assigning one point to the ideal level while 0 points to the intermediate or poor level for each metric.

The partial population-attributable risk fraction was calculated to estimate the percentage of premature deaths that would be avoided if all people had been with optimum cardiovascular health (scores 10–14), assuming causal associations.[33] We used the pooled HRs estimated from three cohorts and population prevalence from the CKB study, considering that the CKB study recruited participants from ten regions of China but the other two cohorts each recruited participants from one city and with less representativeness. Analyses within cohorts were performed by SAS software version 9.4 (SAS Institute, Cary, NC, USA), and meta-analyses were conducted by STATA software version 14.0 (StataCorp, College Station, TX, USA). Two-sided *P* values <0.05 were considered statistically significant.

Results

Baseline characteristics

Table 1 shows baseline characteristics in three cohorts. In the Kailuan study, participants were younger, and females only contributed a small proportion of participants; accordingly, non-drinking and ideal behavioral metrics were less prevalent. However, the distributions of ICH score were similar across three cohorts [Supplementary Tables 2–4, http://links.lww.com/CM9/B171]. In total, there were 20,445 (10.3%), 93,826 (47.3%), and 83,893 (42.3%) participants with inadequate (scores 0–6), average (scores 7–9), and optimum (scores 10–14) cardiovascular health. Participants with higher ICH scores were more likely to be younger, female, with higher levels of education, and abstainers, and the ideal level of each ICH metric was more prevalent among those with optimum cardiovascular health. There were modest differences in the distribution of age, gender, education

Table 1: Baseline characteristics of study population in CKB study, DFTJ cohort and Kailuan study.

Characteristics	CKB study ($N=33,666$)	DFTJ cohort ($N=26,980$)	Kailuan study ($N=137,518$)
Age (years)	57.8 ± 10.3	61.7 ± 8.1	48.9 ± 13.5
Female	18,872 (56.1)	15,065 (55.8)	26,530 (19.3)
Married	29,354 (87.2)	24,396 (90.4)	129,697 (94.3)
High school or higher	5743 (17.1)	11,032 (40.9)	35,248 (25.6)
Alcohol consumption			
Never drinking	27,149 (80.6)	19,212 (71.2)	81,892 (59.6)
Former drinking	885 (2.6)	1200 (4.4)	3294 (2.4)
Current drinking	5632 (16.7)	6568 (24.3)	52,332 (38.1)
Ideal cardiovascular health*			
Cigarette smoking	22,824 (67.8)	20,700 (76.7)	84,837 (61.7)
Physical activity	11,250 (33.4)	8715 (32.3)	19,704 (14.3)
Diet	2304 (6.8)	13,049 (48.4)	14,891 (10.8)
Body weight	20,235 (60.1)	15,810 (58.6)	70,659 (51.4)
Blood pressure	6179 (18.4)	5518 (20.5)	28,680 (20.9)
Blood glucose	29,418 (87.4)	12,746 (47.2)	96,501 (70.2)
Blood lipid	32,156 (95.5)	18,449 (68.4)	120,948 (88.0)

Data are shown as mean ± standard deviation or *n* (%). * The ideal level of cigarette smoking was defined as never smokers or former smokers who quitted smoking for no less than 10 years. The ideal level of physical activity was defined as the highest tertile of exercise time in the CKB study and DFTJ cohort and >80 min/week in the Kailuan study. The ideal level of diet was defined as daily vegetable intake, daily fruit intake, and no daily red meat intake in the CKB study and DFTJ cohort and daily salt intakes of <6 g in the Kailuan study. The ideal level of body weight was defined as BMI of 18.5–24.9 kg/m^2. The ideal level of blood pressure was defined as SBP of <120 mmHg and DBP of <80 mmHg without treatment. The ideal level of blood glucose was defined as FBG of <5.6 mmol/L or random blood glucose of <7.8 mmol/L without treatment. The ideal level of blood lipid was defined as LDL-C of <3.4 mmol/L without treatment. BMI: Body mass index; CKB: China Kadoorie Biobank; DBP: Diastolic blood pressure; DFTJ: Dongfeng-Tongji; FBG: Fasting blood glucose; LDL-C: Low-density lipoprotein cholesterol; SBP: Systolic blood pressure.

level, alcohol consumption, and ICH metrics between those included in and excluded from the analyses due to missing information (absolute standardized differences ranged between <0.01 and 0.24; Supplementary Table 5, http://links.lww.com/CM9/B171).

ICH metrics and mortality

During 1,968,854 person-years of follow-up, 20,176 deaths were recorded, and 8164 were from CVD (2565 IHD deaths and 4662 stroke deaths), 3289 were from cancer, and 1112 were from respiratory diseases. All ICH metrics were associated with all-cause mortality, except for LDL-C; nevertheless, the association of LDL-C with mortality was stronger than those of other lipid markers [Supplementary Table 6, http://links.lww.com/CM9/B171]. HRs (95%CIs) comparing participants with optimum *vs.* inadequate cardiovascular health were 0.52 (0.41–0.67) for all-cause mortality, 0.44 (0.37–0.53) for CVD mortality, and 0.54 (0.44–0.66) for respiratory mortality [Table 2]. Although a higher ICH score was associated with lower cancer mortality in the DFTJ cohort [Supplementary Table 7, http://links.lww.com/CM9/B171], the pooled HR across three cohorts was not statistically significant (HR 0.86; 95% CI 0.64–1.14). A higher ICH score was also associated with lower IHD and stroke mortality. Dose-response meta-analyses showed that the ICH score was nonlinearly associated with CVD and stroke mortality ($\chi^2 \geq 5.49$, P for nonlinearity ≤ 0.019) while was linearly associated with all-cause, IHD, and respiratory mortality ($\chi^2 \leq 2.28$, P for nonlinearity ≥ 0.130; Supplementary Figure 2, http://links.lww.com/CM9/B171). Given causal relations, 25.0% (17.3–32.4%), 31.9% (23.1–40.2%), and 24.8% (2.9–44.4%) of all-cause, CVD, and respiratory mortality would be avoided if all individuals followed optimum cardiovascular health (ICH scores 10–14).

Stratified analyses showed consistent associations between ICH and mortality among subgroups [Supplementary Tables 8–11, http://links.lww.com/CM9/B171]. However, the HRs (95% CI) of CVD mortality comparing the optimum *vs.* inadequate cardiovascular health were 0.32 (0.28–0.36) among those aged <60 years, which was stronger than 0.53 (0.38–0.75) among those aged ≥60 years ($t=3.12$, $P_{\text{between-group}}=0.036$). Results remained comparable when excluding participants dying within the first three years of follow-ups, using the original AHA's definition of ICH score, excluding participants with prevalent emphysema or chronic bronchitis at baseline, adjusting for the family history of major noncommunicable diseases, using the multiple imputation to account for missing variables, or using the 7-point ICH score [Supplementary Table 12, http://links.lww.com/CM9/B171 and Supplementary Figure 3, http://links.lww.com/CM9/B171].

Interaction between behavioral and medical scores

Figure 1 shows that both higher behavioral and medical scores were independently associated with lower all-cause and CVD mortality, whereas only a higher behavioral score was associated with lower respiratory and cancer mortality. No significant interactions were found between the behavioral and medical scores ($t < 1.99$, $P_{\text{between-group}} \geq 0.086$; Figures 2 and 3 and

Table 2: Associations between ICH score and all-cause and cause-specific mortality: pooled results of three prospective cohorts in Chinese adults.*

	ICH score			
Causes of mortality	**0–6 points**	**7–9 points**	**10–14 points**	**1-point increase**
All-cause mortality				
Person-years	201,739	934,890	832,225	1,968,854
Number of events	3014	11,249	5913	20,176
HR (95% CI)	Reference	0.73 (0.60–0.88)	0.52 (0.41–0.67)	0.88 (0.84–0.92)
CVD mortality				
Person-years	141,745	655,686	589,738	1,387,169
Number of events	1475	4674	2015	8164
HR (95% CI)	Reference	0.69 (0.58–0.82)	0.44 (0.37–0.53)	0.85 (0.83–0.87)
IHD mortality				
Number of events	466	1422	677	2565
HR (95% CI)	Reference	0.67 (0.56–0.81)	0.44 (0.39–0.50)	0.84 (0.83–0.86)
Stroke mortality				
Number of events	848	2750	1064	4662
HR (95% CI)	Reference	0.71 (0.64–0.79)	0.44 (0.40–0.49)	0.85 (0.83–0.86)
Respiratory disease mortality				
Number of events	195	612	305	1112
HR (95% CI)	Reference	0.70 (0.59–0.82)	0.54 (0.45–0.66)	0.89 (0.86–0.92)
Cancer mortality				
Number of events	412	1782	1095	3289
HR (95% CI)	Reference	0.96 (0.77–1.21)	0.86 (0.64–1.14)	0.96 (0.93–1.00)

* Models were adjusted for age, gender, region (only adjusted in CKB study), marital status, education level, income level (adjusted in CKB and Kailuan studies), occupation (only adjusted in CKB study), and alcohol drinking. Results from three cohorts were pooled using random-effects models of meta-analyses. CI: Confidence interval; CKB: China Kadoorie Biobank; CVD: Cardiovascular disease; DFTJ: Dongfeng-Tongji; HR: Hazard ratio; ICH: Ideal cardiovascular health; IHD: Ischemic heart disease.

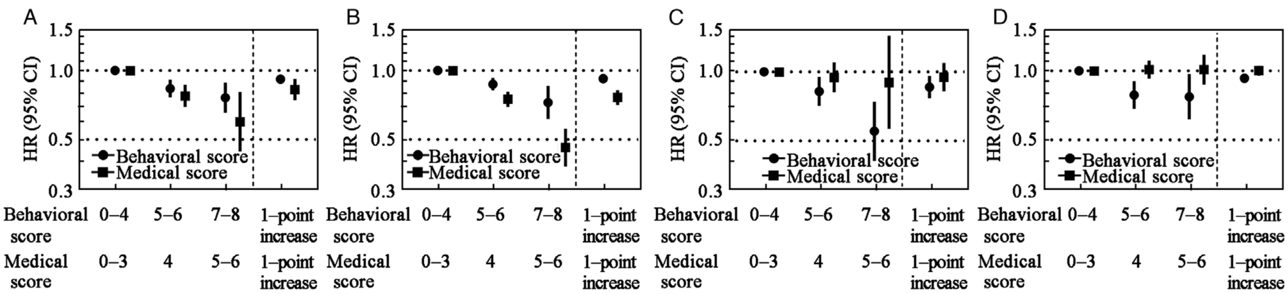

Figure 1: Independent associations of behavioral score and medical score with all-cause (A), cardiovascular disease (B), respiratory disease (C), and cancer mortality (D): pooled results of three prospective cohorts in Chinese adults. The model adjusted for age, gender, region, marital status, education level, income level, occupation, and alcohol drinking, as well as behavioral score and medical score mutually. CI: Confidence interval; HR: Hazard ratio.

Supplementary Figure 4, http://links.lww.com/CM9/B171). Compared with those with behavioral scores of 0–4, participants with the behavioral scores of 7–8 were associated with lower all-cause mortality across all medical score groups, and the HRs (95% CIs) were 0.77 (0.64–0.93), 0.79 (0.62–1.01), and 0.73 (0.65–0.82) for those with the medical scores of 0–3, 4, and 5–6, respectively. Similar patterns were also observed in cause-specific mortality. Additionally, a higher medical score was associated with all-cause and CVD mortality across all behavioral score groups, for example, HRs (95% CIs) of all-cause mortality comparing participants with the medical scores of 5–6 *vs*. 0–3 were 0.62 (0.44–0.88), 0.59 (0.46–0.75), and 0.56 (0.38–0.83) for those with the behavioral scores of 0–4, 5–6, and 7–8, respectively. Results for IHD and stroke mortality were similar to those for CVD mortality.

Discussion

In these three Chinese cohorts with about 2 million person-years of follow-up, optimum cardiovascular health was associated with lower all-cause, CVD, and respiratory mortality. Besides, better behavioral and medical health were independently associated with lower all-cause and CVD mortality; however, only better behavioral health was associated with lower cancer and respiratory mortality. No significant interactions between behavioral and medical health were observed.

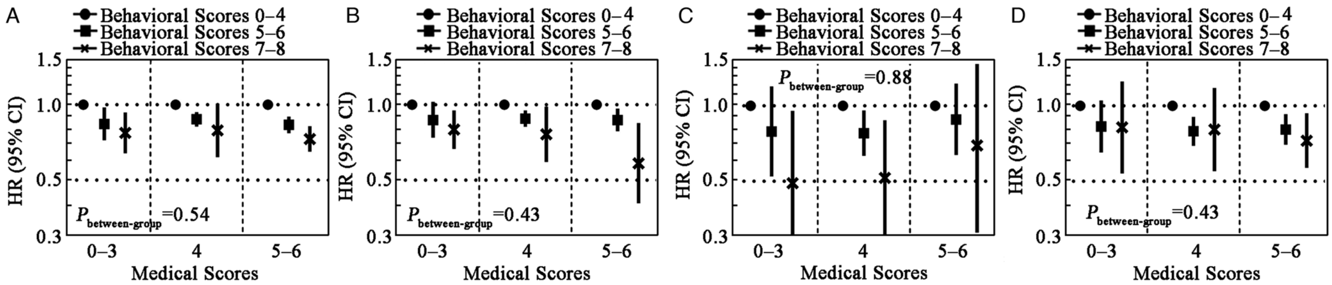

Figure 2: Associations of the behavioral score with all-cause (A), cardiovascular disease (B), respiratory disease (C), and cancer mortality (D) across participants with different medical scores: pooled results of three prospective cohorts in Chinese adults. $P_{\text{between-group}}$ was derived from the meta-regression, which indicated whether the difference in HR associated with a 1-point increase of the score across groups was statistically significant. CI: Confidence interval; HR: Hazard ratio.

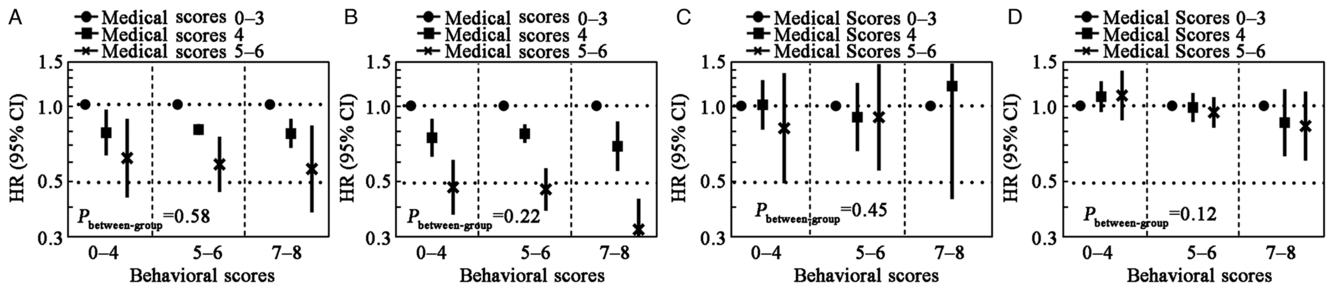

Figure 3: Associations of the medical score with all-cause (A), cardiovascular disease (B), respiratory disease (C), and cancer mortality (D) across participants with different behavioral scores: pooled results of three prospective cohorts in Chinese adults. $P_{\text{between-group}}$ was derived from the meta-regression, which indicated whether the difference in HR associated with a 1-point increase of the score across groups was statistically significant. Among participants with behavioral score of 7-8 points, the HR of medical score of 5-6 points for respiratory disease mortality exceeded the upper range of the y-axis, and the HR (95% CI) was 1.56 (0.78–3.09). CI: Confidence interval; HR: Hazard ratio.

The results were largely consistent with previous studies. A recent meta-analysis with >0.5 million participants reported that the highest ICH score category was associated with 45% and 61% lower all-cause and CVD mortality.[3] A previous publication from the Kailuan study also found that meeting more ICH metrics was associated with lower all-cause and CVD mortality; however, the study only included participants recruited in 2006 to 2007 and the follow-up duration was too short (median = 4.02 years).[27] Additionally, the associations of ICH with mortality from CVD subtypes or non-CVD diseases have not been extensively studied and the results were inconclusive. Two studies investigated the association between ICH and IHD mortality. The US National Health and Nutrition Examination Survey with 13,312 participants and 576 IHD deaths found the highest ICH score category was associated with 70% lower IHD mortality which was similar to our results,[9] while a Lithuania study with fewer IHD deaths (9209 participants with 342 IHD deaths) found no significant association.[8] For cancer mortality, the US National Health and Nutrition Examination Survey[24] and Cardiovascular Health Study[10] found individuals in the highest ICH score groups were associated with 43% to 58% lower cancer mortality; however, the Aerobics Center Longitudinal Study found no significant association.[22] Similarly, we found that optimum cardiovascular health was associated with a 36% lower risk of cancer mortality in the DFTJ cohort, whereas a null association was observed after pooling the results with the other two cohorts. When separating behavioral and medical metrics, we only found that a higher behavioral score was associated with lower cancer mortality. Moreover, a recent meta-analysis with five studies and >0.5 million participants showed that the highest ICH score groups were associated with a 29% lower cancer risk.[7] Future studies are still warranted to reach a reliable conclusion regarding the association between ICH and cancer mortality. Our study reported associations of ICH with stroke and respiratory mortality for the first time and found participants in the highest ICH score group were associated with 56% and 46% lower risks of stroke and respiratory mortality, respectively. Previous studies also found a higher ICH score was associated with lower risks of stroke[3] and respiratory diseases.[5,6] This is the largest study to investigate the associations of ICH with mortality from subtypes of CVD and non-CVD disease (about 0.2 million participants, 16 times larger than the previous largest study[24]), and the results are robust.

In our study, associations between ICH and mortality were largely consistent in multiple stratified analyses; however, the association between ICH and CVD mortality was stronger among those aged <60 years compared with those aged ≥60 years, which was consistent with previous studies.[3,9] Given the looser targets of blood pressure and blood glucose levels as well as obesity paradox among elders,[34-36] it is advisable to modify the definition of each ICH metric targeting elders.

Both our study and previous studies found that higher behavioral and medical scores were independently associated with lower all-cause and CVD mortality.[37,38] Besides, a previous longitudinal study of 3491 elders also found no interaction between the American Cancer Society behavioral score and AHA medical score on all-cause mortality[10]; however, the sample size was small. Other studies also found no interactions between behavioral and medical scores on incident CVD and diabetes.[39,40] Hence, all individuals should target healthy lifestyles and cardiometabolic conditions regardless of their medical and behavioral health.

With a sufficient sample size and long follow-up duration, we investigated the associations of ICH with all-cause and cause-specific mortality in three Chinese cohorts, as well as the interaction and independent associations of the behavioral and medical scores with mortality. However, several limitations should be acknowledged. First, the definitions of some ICH metrics were modified because of data availability and distribution of characteristics in our study population. Nevertheless, results remained consistent when we used the original AHA's definition. Besides, the definitions of ideal levels of physical activity and diet were different between DFTJ cohort/CKB study and Kailuan study due to data availability, and the results need cautious interpretation. Second, the study sample was not nationally representative, and thus the estimated population-attributable risk fraction should be interpreted cautiously. Third, although we adjusted for major demographic characteristics and alcohol consumption, residual confounding is still possible, and causal inference cannot be made due to the nature of the observational study. Fourth, the participants dying within a mean follow-up of 9.9 years might have serious comorbidities at baseline, which could influence both the ICH metrics and mortality. Although we excluded those with CVD or cancer at baseline and the results remained largely unchanged in the sensitivity analyses of excluding those dying within the first three years or excluding those with prevalent respiratory disease at baseline, there is still the possibility of residual confounding and reverse causation from other unmeasured disease histories. Fifth, we used single-measured ICH metrics and covariates, and demographic and lifestyle information was self-reported. Thus, results might be biased by measurement errors. Sixth, there were modest differences in demographic, behavioral, and medical factors between participants included in and excluded from the analyses due to missing information, and selection bias was possible; however, the results remained consistent when using the multiple imputation to impute missing information.

In conclusion, meeting more ICH metrics was associated with lower all-cause, CVD, and respiratory mortality in the Chinese. Healthier behaviors and medical conditions were independently associated with lower all-cause and CVD mortality, and no interaction was observed. Associations of ICH with mortality from non-CVD or subtypes of CVD and the interaction between behavioral and medical metrics need further validation in other populations.

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Conflicts of interest

None.

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