The combined healthy lifestyle score is a protective factor for cardiovascular disease: a representative national cohort study in Taiwan

Ming-Chieh Tsai
Mackay Memorial Hospital
Tzu-Lin Yeh
Mackay Memorial Hospital Hsinchu
Hsin-Yin Hsu
Mackay Memorial Hospital
Le-Yin Hsu
National Taiwan University
Chun-Chuan Lee
Mackay Memorial Hospital
Po-Jung Tseng
Taoyuan Armed Forces General Hospital
Kuo-Liong Chien (klchien@ntu.edu.tw)
National Taiwan University College of Public Health

Original investigation

Keywords: Healthy lifestyle scores, cardiovascular disease, World Cancer Research Fund (WCRF) and the American Institute for Cancer Research (AICR), Life's Simple 7, integrated discriminative improvement, net reclassification improvement

Posted Date: January 15th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-144452/v1

Abstract

Background

The protective effect of different healthy lifestyle scores for the risk of cardiovascular disease (CVD) was reported but the comparisons of performance were lack. We compared the performance measures of cardiovascular diseases from different healthy lifestyle scores among adult Taiwan.

Methods

We conducted a nationwide prospective cohort study of 6042 participants (median age 43 years, 50.2% women) in Taiwan's Hypertensive, Hyperglycemia and Hyperlipidemia Survey, 2002 who were free of CVD at baseline. Simple and weighted Taiwan healthy lifestyle score was defined as combination of normal body mass index, Mediterranean diet, adequately physical activity, not smoking and regular healthy drinking and each dichotomous lifestyle factor. World Cancer Research Fund and the American Institute for Cancer Research (WCRF/AICR) cancer prevention recommended lifestyle and Life's Simple 7 following the guideline definition. The incidence of cardiovascular disease incidence among the 4 healthy lifestyle score each divided into 4 groups based on scores were estimated.

Results

During a median 14.3 years follow-up period, totally 520 cases developed CVD events. In multivariate-adjusted Cox proportional hazard models, adherence to highest category compared with lowest one of simple Taiwan lifestyle score for hazard ratio 0.43 (95% confidence interval [CI] 0.2, 0.94) and weighted Taiwan lifestyle score for 0.44 (95%CI 0.28, 0.68) were independently and significantly. In addition, age played a significant effect modifier for the protective effect of healthy lifestyle scores for CVD risk. Specifically, when the simple and weighted Taiwan healthy lifestyle score were added to the classical model, the Harrell's C-statistic increasing from 0.85 to 0.86 (95% confidence interval [CI], 0.84, 087; Pdiff=0.02) in both lifestyle scores. The performance measures by integrated discriminative improvement showed significant increasing after adding simple Taiwan healthy lifestyle score (integrated discriminative improvement: 0.51, 95% CI 0.16, 0.86, P=0.002) and weighted Taiwan lifestyle score (integrated discriminative improvement: 0.38, 95% CI 0.01,0.74, P=0.021) information.

Conclusions

We demonstrated that healthy lifestyle scores with an inverse association with CVD, and the reduction of CVD risk was more for young adults than for old adult. Further investigations to study the mechanism of lifestyle role on CVD prevention are warranted.

Background

Cardiovascular diseases are the leading noncommunicable diseases and were associated with an estimated 17.9 million deaths (31% of the global annual mortality) in 2016;[1, 2] moreover, 85% of the deaths was attributed to coronary heart disease-related myocardial infarctions and stroke (7.4 and 6.7 million, respectively). Recent research has explored whether a combination of multiple healthy lifestyle behaviors, rather than a single behavior, facilitates processes beneficial to the prevention of cardiovascular disease, and found a decreased incidence of overall cardiovascular disease (range 0.22–0.45) than with the maximal numbers of non-optimal interventions.[3–25] In 2007, the World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) reported lifestyle recommendations[26] to potentially reduce cancer risk in adults based on a comprehensive meta-analysis that included more than 500 investigations. The American Heart Association defined "Life's Simple 7" – an evidence-supported effective construct of ideal cardiovascular health with four favorable health behaviors and three health clinical factors, including serum total cholesterol, blood pressure, and no diabetes, to improve the cardiovascular health in the community.[27–34]

The protective effects of a combination of healthy lifestyle factors evaluated as a lifestyle score to determine the CVD risk has been investigated previously, especially in American and European populations. However, it is unclear whether a healthy lifestyle score could reduce the lifetime CVD risk in Asian populations, and the magnitude of the population attribution fraction of the healthy lifestyle score on the CVD incidence is undetermined. Furthermore, the non-weighted healthy lifestyle score, based on the assumption that all lifestyle factors have the same magnitude of effect, potentially leads to a misclassification bias. The impact of the weighted healthy lifestyle score on the CVD incidence has important clinical implications, but there is a lack of evidence on this aspect. The healthy lifestyle score derived from the recommendation of WCRF/AICR has been shown to favorably influence of cancer risk, but there is little evidence on the CVD risk. Moreover, Life's Simple 7 has been proposed to have an inverse association with the CVD risk. Therefore, we were particularly interested in the predictive performance of the combined healthy lifestyle factors, healthy lifestyle score from the WCRF/AICR, and Life's Simple 7 for the CVD risk. Furthermore, age as a potential effect modifier on the association between healthy lifestyle score and CVD risk has been studied in a

secondary data,[35] although there has been no validation in research from primary analysis on whether targeting younger adults for primordial prevention of CVD would be more feasible compared with this intervention in older adults.

Accordingly, this study sought to assess whether healthy lifestyle scores, as captured by a simple and weighted combination of nonobese body mass index (BMI), healthy dietary quality, physical activity, non-smoking and adequate drinking, are associated with the CVD risk in a national representative cohort of Taiwanese adults. Furthermore, the performance ability among the four healthy lifestyle scores for predicting the CVD risk were compared.

Methods

Participants

2002 Taiwan Survey of Hypertensive, Hyperglycemia, Hyperlipidemia Survey (2002 TwSHHH) was a national representative prospective cohort was established in 2002. Briefly, participants of the TwSHHH cohort were included on the basis of multistage, stratified, random sampling from the National Health Interview Survey, which recruited 7578 individuals (age ≥ 15 years) and obtained detailed information from a face-to face questionnaire, anthropometric measurements, and blood sample analyses, which has been described in previous articles[36, 37]. Each participant's baseline data that were collected from March 11, 2002 to August 10, 2002 were linked to the Taiwan Statistics of Causes of Death and National Health Insurance Research Database (NHIRD) until December 31, 2015, and were obtained from a universal, single-payer, and compulsory health insurance system that covers 99% of the 23 million residents of Taiwan, with diseases identified according to the International Classification of Disease-9 and 10 (ICD-9 and ICD-10) codes. All eligible participants in this study were excluded if recruited prior to the enrollment date of the 2002 Taiwan's Triple High Survey and if they: (1) were younger than 20 years; (2) had a pregnancy within the previous 1 year; (3) had a recorded history of coronary artery disease and ischemic stroke in the National Health Insurance system; and (4) had missing data for identical numbers linked to the Taiwan National Health Interview Survey or National Health Insurance Research Database. A total of 6048 participants were included in the final analysis dataset used for the current analyses. Informed consent was obtained from each participant. The protocol was reviewed and approved by the Research Ethics Committee of National Taiwan University Hospital.

Assessment of healthy lifestyle factors

The body mass index (BMI) was calculated as the weight in kilograms divided by the square of height in meters from self-reported data in 2002 and participants were categorized as underweight (BMI < 18.5), normal weight (18.5 ≤ BMI < 25), obesity I (25 ≤ BMI < 30), obesity II (30 ≤ BMI < 35), obesity III (35 ≤ BMI < 40), and obesity IV (40 ≤ BMI) according to the recommendations of the World Health Organization.

Data used to generate the healthy diet patterns were derived from a simplified food frequency questionnaire with 20 items of food. We used the alternative Mediterranean diet score as our healthy dietary score (supplement), which was calculated by the frequency of intake and added scores across all 11 components of the 17 primary criteria contained in the Mediterranean dietary score for the following items39: fresh vegetables, legumes, fresh fruits, dairy products (milk, goat's milk, fermented milk, cheese, yogurt, Yakult), grains (rice or noodle), meat (beef, pork, goat, chicken), fish, eggs, sweets (cookies, candies, chocolate, cakes, bread, ice cream, milkshake), nonalcoholic beverages (cola, soda or sweet-beverage), and saturated lipid (burger, French frizzed, pizza). Participants were further classified according to the different levels of the alternative Mediterranean diet score (0–3, 4–5, 6–7, and 8–11 points). Participants with an alternative Mediterranean healthy diet score of 6 or more than 6 points were assigned to the adherence of healthy diet group, whereas those with scores less than 6 were assigned to the nonadherence of healthy diet group. Physical activity during the past 2 weeks were categorized as adequate active (1–50, 51–100, and 101–150 minutes/week) and nonoptimal physical activity, including inactive (0 minute/week) or overactive (> 150 minutes/week) grading (supplemental table 3). Smoking status was categorized as current smoking ≥ 20 years, current smoking < 20 years, quit smoking < 1 year, quit smoking ≥ 1 year, and never smoking (supplemental table 4). The participants were questioned about the usually drinking status and categorized as having frequency alcohol consumption (dinking every day with undrunk, half-drunk, or drunk status; drinking per 2 days with half-drunk or drunk status; and drinking once a week, with drunk status) or few (drinking less than once a week or drinking per 2 days, with an undrunk status) or no alcohol consumption (supplemental table 5). A detailed description of the questions and definition on ideal BMI, healthy diet, adequate physical activity, non-smoking status, and frequency alcohol consumption has been presented in supplemental tables 6 was based on the current literature, recommended guidelines but also based on levels realistically obtainable within the general population.

Healthy lifestyle scores

We created a simple pragmatic combined healthy lifestyle score. We created a healthy lifestyle score to sum each dichotomous lifestyle factor as "optimal" versus "nonoptimal" as follows: normal BMI (BMI < 25 kg/m2) versus obese (BMI ≥ 25 kg/m2), alternative Mediterranean diet 6 or higher points versus less than 6 points, adequate physical activity (1–150 min/week) versus non-optimal physical activity (0 or > 150 min/week), never smoking versus current or quit smoking, and frequent drinking versus few or no drinking. The participants received 1 point for each optimal criterion met, and points were summed to obtain a Taiwan healthy lifestyle score ranging from 0 (nonoptimal) to 5

(optimal). A weighted healthy Taiwan healthy lifestyle score also was created, where each dichotomous lifestyle factor was first weighted according to its independent magnitude of effect (e.g., beta coefficient adjusted for the other dichotomized lifestyle factors) on cardiovascular disease risk, and ranged from 0 to 17.

In accordance with the WCRF/AICR 2018 definition, the WCRF/AICR lifestyle score was created, which was a composite numerical measure of the adherence of health lifestyle and consisting of 7 main components, with each score based on a 0, 0.25, 0.5, and 1 scale representative from less healthy to most healthy. We defined the WCRF/ACIR healthy lifestyle score as the sum of scores across of all seven main components, including healthy weight, physically active, a diet rich in wholegrains, vegetables, fruit, and beans, and limiting consumption of “fast foods”, red and processed meat, sugar-sweetened drinks and alcohol. Based on the 2019 AHA update criteria of cardiovascular health, the Life's Simple 7 in our study included four core health behaviors (BMI, healthy diet (supplemental table 9), physical activity and non-smoking) and three health factors (cholesterol, blood pressure, and glycemic control). (supplemental tables 10). Each healthy heart behavior and factors providing 2 points for an ideal metric, 1 point for an intermediate metric, and 0 points for a poor metric were added to obtain the Life's Simple 7 score, ranging from 0 to 14.

Important covariates

At baseline, participants reported on sociodemographic factors and medical history, including educational level, monthly income, marital status, menopause status, history of estrogen exposure, and parental history of cardiovascular disease. Additionally, a history of the diagnosis of diabetes mellitus, hypertension and hyperlipidemia at baseline were obtained based on the measurement in 2002 or by ICD-9 or prescription of drugs from NHIRD prior to enrolled date. Diabetes at baseline was defined as a fasting serum glucose ≥ 126 mg/dL and hemoglobin A1c ≥ 6.5 mg/dL or records with two consistent diagnosis of diabetes by the ICD-9 codes or prescription of antidiabetic drugs for more than 28 days in data from the NHIRD prior to the enrollment date. Hypertension was defined as systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg or records with two repeated diagnoses of hypertension or prescription of anti-hypertensive drugs for more than 28 days in data obtained from the NHIRD prior to enrollment date. Data on the use of lipid-lowering agent and aspirin were obtained from the drug register and defined as yes while prescriptions of more than 28 days prior to the enrolled date were included. Abdominal obesity was indicated as a waist circumference ≥ 80 cm in women and ≥ 90 cm in men. The adjusted factors included systolic blood pressure, diastolic blood pressure, and serum biomarkers obtained during the 2002 interview. The biomarkers comprised fasting glucose, glycated hemoglobin, triglyceride, and non-high-density lipoprotein cholesterol (HDL) as the continuous variables.

Outcome ascertainment and prospective follow-up

Follow-up information was obtained from the NHIRD and the Taiwan Cause of Death Register for fatal outcomes by record linkage using the personal identification numbers assigned to every citizen on Taiwan. ICD-9 codes were used to identify cardiovascular disease, such as coronary artery disease (ICD-9 codes 410–411, 414 and V45.81-82) or ischemic stroke (ICD-9 codes 433–436, 4371, 4379), with the first hospitalization with a diagnosis of the abovementioned interest events and the event date defined as the first date of hospitalization (Supplemental Table 1). We ascertained the occurrence of coronary artery disease- and stroke-related deaths from the death certificate. All participants were flagged for death at the department of Household Registration, with coded death certificates using the ICD-9 codes. The diagnoses of coronary artery disease and ischemic stroke were made by the treating physicians, based on a clinical assessment and examinations as considered relevant by the clinician in charge of treatment.

Statistical Analyses

Participants were categorized into four groups among each healthy lifestyle scores, based on the simple and weighted Taiwan healthy lifestyle score, the WCRF/AICR healthy lifestyle score, and Life's Simple 7 score (Supplemental Table 12). The continuous variables are presented by the mean, standard deviation, or median levels; categorical data are presented in a contingency table with ANOVA to test for differences among quintiles. Multivariate Cox regression models were constructed for the combined health lifestyle scores, with the lowest score category used as the reference category (Supplemental Table 13). The linear trend test for lifestyle scores was performed by treating the number of low-risk factors as a continuous variable. The population attributable risk (PAR) was estimated using hazard ratio (HRs) obtained from the different Cox regression models in our cohort with that in the fully adjusted model. We tested potential effect modifiers based on the age category (< 60 and ≥ 60 years) by using the likelihood ratio test to compare models with and without a cross-product term.

To further investigate the role of a combination of healthy lifestyle factors to predict the CVD risk, we compared the four models with the healthy lifestyle score and tested the prediction performance using the calibration and discrimination abilities based on the Hosmer–Lemeshow statistic,[38] comparisons of the Harrell C-index of survival data,[39–41] calibration curves, the net reclassification improvement (NRI), and integrated discrimination improvement (IDI) statistic.[42] All statistical tests were two-tailed with a type I error. Statistical

significance was considered at two-sided *p*-values < 0.05. The SAS version 9.4 (SAS Institute, Cary, NC, USA) and Stata version 12 (Stata Corporation, College Station, TX, USA) were used for statistical analysis.

Results

The final analytic sample included data obtained during a mean follow-up of 12.5 years, with 520 (8.6%) new cases of cardiovascular events and 20 confirmed CVD-related deaths (3.8%) that occurred during the study (Supplemental Fig. 1). The baseline characteristics of the study participants (3012 men [49.8%], 3036 women [50.2%]) included a mean (SD) age of the population at baseline of 44.9 ± 16 years, whereas the mean age at CVD diagnosis was 63.0 ± 12.8 years. The general baseline characteristics according to the number of healthy lifestyles in the simple Taiwan healthy lifestyle score, weighted Taiwan healthy lifestyle score, WCRF/AICR lifestyle score, and Life's Simple 7 score are presented in Table 1 and Supplemental Table 14.

Each lifestyle factor and the CVD risk after multivariable adjustments among each lifestyle factor and the partial population attributable fraction (95% confidence interval [CI]) are shown in Supplementary Table 15. The participants with the highest healthy lifestyle scores had a significantly higher survival rate free from the CVD risk in the simple and weight Taiwan healthy lifestyle scores and Life's Simple 7, although this benefit was not observed for the WCRF/AICR lifestyle score (Table 2, Supplemental Table 16, and Supplemental Fig. 2). In multivariable-adjusted analyses, adults with adherence to the highest number of lifestyle factors compared with those who had adherence to the lowest numbers had a lower incidence of CVD events based on the simple Taiwan healthy lifestyle score (hazard ratio [HR] 0.43, 95% CI 0.2–0.94), weighted Taiwan healthy lifestyle score (HR 0.44, 95% CI 0.28–0.68), and Life's Simple 7 (HR 0.60, 95% CI 0.29–1.24); moreover, a similar association was observed in the *p* for trend test (Table 2, Fig. 1, and Supplemental Fig. 3). However, no inverse and graded association were noted between the WCRF/AICR lifestyle score and CVD risk, both in the Cox regression analysis and the *p* for trend test. The PAR (95% CI) for participants with higher healthy lifestyle scores was estimated to be 38.8 (19.2–53.6), 34.3 (17.8–47.4), and 24.5 (3.1–41.2) for the simple Taiwan healthy lifestyle score, weighted Taiwan healthy lifestyle score, and Life's Simple 7 score, respectively. These findings suggested that the majority of CVD may be preventable with adherence to a healthy lifestyle.

When we stratified the study population by age at baseline < 60 or ≥ 60 years, a significantly inverse association between the healthy lifestyle scores and the CVD risk for a given number of lifestyle factors in all four healthy lifestyle scores (Table 3) persisted, although participants younger than 60 years had a greater reduction of CVD risk than those aged 60 years or older (Supplemental Fig. 4). Thus, the analyses indicated that the protective effect of healthy lifestyle scores for CVD incidence indeed varied by the age in adult participants. In sensitivity analysis, a similar result was observed (Supplemental Table 17).

Assessment Of Model Performance Of Four Healthy Lifestyle Scores

The Hosmer–Lemeshow test statistic indicated an acceptable goodness-of-fit of the calibration ability, and the model was well calibrated for 12.5-year CVD risk prediction based on the calibration in four healthy lifestyle scores (Table 4 and Supplemental Fig. 5). With regard to the discriminative ability of different healthy lifestyle scores to predict the CVD risk, the Harrell C-statistics significantly increased from 0.85 to 0.86 (P_{diff}=0.02) for the simple Taiwan healthy lifestyle score and significantly increased from 0.84 to 0.87 (P_{diff}=0.003) for the weighted Taiwan healthy lifestyle score (Supplemental Fig. 6). Moreover, we found that the performance measures evaluated by the IDI showed significant improvement of 0.38% (95% CI; 0.01, 0.74; *p* = 0.021) for the simple Taiwan healthy lifestyle score and 0.51% (95% CI; 0.16, 0.86; *p* = 0.002) for the Taiwan healthy lifestyle score. The net reclassification improvement was statistically significant for the Mediterranean diet-related healthy lifestyle score (0.03; 95% CI 0.01–0.05; *p* = 0.004) and the Taiwan healthy lifestyle score (0.04; 95% CI 0.02–0.06; *p* < 0.001). However, the Harrell C-statistics, IDI, and NRI showed no significant difference for the WCRF/AICR healthy lifestyle score or Life's Simple 7 score.

Discussion

In this representative adult Taiwanese study population, 38.8% of all CVD events may have been avoided had all participants adhered to a healthy lifestyle with regard to normal weight, healthy Mediterranean diet, regular physical activity, non-smoking, and adequate healthy drinking. Moreover, we noted the protective effect of the simple and weighted Taiwan healthy lifestyle score and Life's Simple 7 score for CVD risk reduction. Furthermore, we noted that the age of adult participants had a modifier effect on the inverse association between the healthy lifestyle scores and CVD risk. Younger and hypertension-free participants who adopted an optimal lifestyle derived greater benefits than the older adult population.

The findings of this study are consistent with those of previous cohort studies in European, US, and Asian populations and suggested a protective effect of healthy lifestyle scores and the CVD risk in an extensive Chinese general population. However, previous cohort studies had limitations with regard to the analysis of adjusted covariates, including age, sex, socioeconomic status, parental history of CVD, and medical

history at baseline, although a few studies adjusted the analysis for clinical factors.[4, 6, 13, 14, 19–21, 23] In this study, although aspirin and lipid-lowering agents were not included in our adjusted models because of their low prevalence among the study population at baseline, we estimated the HR after adjusting the models for age, sex, socioeconomic, and health status at baseline and for clinical factors, such as blood pressure, fasting glucose level, triglyceride level, and non-high-density lipoprotein cholesterol level. All of these results from studies including clinical factors as adjustment covariates imply that the combined lifestyle interventions had an additional benefit for decreasing the CVD incidence by mechanisms other than those associated with the controlling of blood pressure, glucose, and lipid levels.

On a comparison of the weighted lifestyle score and the simple lifestyle score to examine the assumption of each lifestyle factor with the same magnitude effect of the CVD risk by the area under curve, the IDI and NRI demonstrated similar predictive performance for the CVD incidence. This result was consistent with those from previous studies on a healthy lifestyle and risk of heart failure,[3] with relevance as the first study of the weighted healthy lifestyle score and CVD risk. The similar results for both lifestyle scores might imply that there was no additional benefit of focusing on a single or two healthy behaviors than that of the integration of all healthy lifestyle factors. Moreover, adopting an overall healthy lifestyle rather than a strong emphasis on a particular lifestyle was an optimal strategy to improve cardiovascular health.

Multiple observational studies have reported an inverse association between adherence to a high WCRF/AICR lifestyle score and various cancer incidences.[43–46] Previous studies of the association between greater adherence to the WCRF/AICR lifestyle score and the CVD risk factors were limited and have yielded inconsistent findings. A cross-sectional study reported that an increasing adherence to the WCRF/AICR recommendation decreased the incidence of metabolic syndrome,[47] whereas another study observed that it was associated with higher serum levels of thrombomodulin and thrombopoietin that might increase the CVD risk.[48] To our knowledge, this is the first prospective cohort study reported the association between the WCRF/AICR lifestyle score and CVD risk although the analyses demonstrated nonsignificant associations.

The association between Life's Simple 7 and CVD risk in observational studies has been confirmed in repeated re-analyses.[49–58] However, in this study wherein several clinical risk factors and biomarkers were adjusted, the cardiovascular protection conferred from a higher Life's Simple 7 score was attenuated. This decline in the preventive effect against CVD incidence among Life's Simple 7 score implies that the protective benefits derived more from the clinical risk factors than from lifestyle factors, which drive the score. This shifts the focus from primordial prevention to the primary prevention of clinical risk factors and toward the targeting of individuals with higher short-term, rather than a long-term, CVD risk.

Compared with different healthy lifestyle scores, the Taiwan lifestyle score might be more suitable for primordial prevention in populations without clinical risk factors. The different CVD risk performances might be explained by the different definitions of healthy diet, physical activity, and the lack of an alcohol consumption or smoking component. The Mediterranean diet evaluated in the Taiwan lifestyle score was defined as comprising fish as an optimal food for CVD protection but with limited egg and dairy in the daily dietary intake. Moreover, the Taiwan lifestyle score defined regular adequate alcohol consumption as part of an optimal lifestyle. However, the WCRF/AICR lifestyle score considers no alcohol intake to be an ideal lifestyle whereas the Life's Simple 7 does not take the amount of alcohol consumption into consideration. Additionally, the non-smoker or cessation of smoking status contributed to the Taiwan healthy lifestyle score and Life's Simple 7 score, but was not calculated in the WCRF/AICR lifestyle score.

Multiple reasons might explain the benefits derived from a healthy lifestyle among the younger population more than that in the elderly which was observed in this study. First, aging is an original strong risk factor for atherosclerosis. Research had reported that even in individuals with an ideal modifiable lifestyle and healthy status, the development of a high CVD risk still occurs among people in the age range of 65–75 years depending on different racial influences.[59] A 60% of the 10-year predicted atherosclerotic CVD risk was attributable to age alone. Additionally, the magnitudes of causal association between lifestyle and CVD risk might be reduced when including age as a significant covariates.[60] Second, a legacy effect of CVD risk from nonoptimal behavioral factors leading to a subsequently persistent pathological change even in individuals who have an optimal lifestyle has been reported recently.[61] Elders have a longer lifetime to experience a nonoptimal lifestyle than younger individuals, and the legacy effect of nonoptimal lifestyle behaviors should be considered. Finally, people with chronic diseases would have a stronger motivation to maintain a healthy lifestyle. However, the higher prevalence of chronic diseases among the elderly population may play a role as a potential confounder in the CVD incidence that reduces the protective effect against CVD obtained from a healthy lifestyle .

The clinical implications include the identification of unhealthy lifestyle factors among young and middle-aged adults and that aggressively healthy lifestyle interventions are crucial for improving the population cardiovascular health. Additionally, among populations with low short-term risks, healthy lifestyle scores in the absence of clinical risk factors independently provided additional important information about the long-term CVD risk and overall CVD burden. Furthermore, the simple Taiwan healthy lifestyle score as well as the weighted score was a useful tool for application in primary health services, even at home and without the clinical setting, which may broaden public health screening

without the need for laboratory-based measures or may have implications for the development of health policies with different strategies from that of the primordial and primary prevention of CVD.

This study has several strengths. The TWsHHH evaluated a population of middle-aged adult with low prevalence of clinical risk factors in a national representative cohort with little loss to follow-up over 12.5 years and obtained information on the primary lifestyle habits and the direct effect measures of clinical risk factors and biomarkers. Second, the protection from the healthy lifestyle score on the CVD risk was validated in an Asian population as a primordial preventive policy in response to the 2025 global target of the World Health Organization among Western countries that extends to the Asian population. Additionally, to our knowledge, this is the first research study that estimated the CVD risk specifically from the WCRF/AICR recommended lifestyle score and undertook a comparison of the predictive performance for CVD risk among different healthy lifestyle scores, including biomarkers. Finally, age as effect modifier between the association was demonstrated by the primary data validation.

Nonetheless, several study limitations should be mentioned. The Taiwan healthy lifestyle score was assessed in the TWsHHH cohort but lacks external data validation. Additionally, lifestyle factors recorded at the baseline without repeated assessments confers a potential for non-differential misclassification in the study. Nevertheless, if the association between the healthy lifestyle score and the CVD risk was significant with regard to a misclassification bias, the true relative risk between these factors should be more effective due to the subsequent repeated measurements of exposure. Finally, although the Mediterranean diet was demonstrated to significantly reduce the CVD incidence, the Western diet score might not be suitable for the Asian dietary patterns. Thus, the development of an Asian healthy diet score could improve identification of the differences.

Conclusion

Adherence to a high combined healthy lifestyle score plays an important role in the primary prevention of CVD, especially in younger adults with low short-term risks. The simple and weighted Taiwan healthy lifestyle scores can be more effective and predictive of CVD risk reduction than the WCRF/AICR lifestyle score and Life's Simple 7 score in the adult Taiwanese population. Further investigation of the mechanism of CVD prevention based on healthy lifestyle scores independent of the clinical factors is necessary to validate these findings.

Abbreviations

CVD
cardiovascular disease
BMI
body mass index
WCRF/AICR
World Cancer Research Fund and the American Institute for Cancer Research
NHIRD
National HealthfInsurance Research Database
HR
hazard ratios
IDI
integrated discriminative improvement
NRI
net reclassification improvement

Declarations

Ethics approval and consent to participate

This study was approved by the Ethical Review Board of National Taiwan University Hospital (201901103W). Informed consent of the study participants was not required because the dataset used in this study consists of de-identified secondary data released for research purposes.

Consent for publication

Not applicable

Availability of data and materials

The datasets generated and/or analyzed during the current study are not

publicly available due to the policy declared by "**H_BHP_TWHHH _Database" (https://dep.mohw.gov.tw/dos/lp-3147-113-5-20.html)"** but are available from the corresponding author on reasonable request.

Competing interests

All other authors have no potential conflicts of interest relevant to this article in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Funding

Not applicable

Authors' contributions

All authors have contributed significantly, and that all authors are in agreement with the content of the manuscript: **Conception/Design**: Kuo-Liong Chien, Ming-Chieh Tsai; **Collection and/or assembly of data**: All authors; **Data analysis and interpretation**: Ming-Chieh Tsai, Tzu-Lin Yeh,, Hsin-Yin Hsu, Le-Yin Hsu; **Manuscript writing**; Ming-Chieh Tsai, Tzu-Lin Yeh, Hsin-Yin Hsu1; **Final approval of manuscript**: All authors.

Acknowledgements

Not applicable

Authors' information (optional)

Ming-Chieh Tsai1,2,3, Tzu-Lin Yeh1,4, Hsin-Yin Hsu1,5, Le-Yin Hsu1, Chun-Chuan Lee2, Po-Jung Tseng6, Kuo-Liong Chien1,7

1 Institute of Epidemiology and Preventive Medicine, College of Public Health, National Taiwan University, Taipei City, Taiwan. Room 517, No.17 , Xu-Zhou Rd., Taipei, Taiwan 10055

2.Division of Endocrinology and Metabolism, Department of Internal Medicine, Taipei Mackay Memorial Hospital, No. 92, Section 2, Zhongshan North Road, Taipei City, Taiwan 10449

3.Department of Medicine, Mackay Medical Collage, No. 46, Sec. 3, Zhongzheng Rd., Sanzhi Dist., New Taipei City 25245, Taiwan

4. Department of Family Medicine, Hsinchu MacKay Memorial Hospital, No. 690, Section 2, Guangfu Road, East District, Hsinchu City, Taiwan 30071

5 Department of Family Medicine, Taipei MacKay Memorial Hospital, 10449, No. 92, Section 2, Zhongshan North Road, Taipei City, Taiwan 10449

6 Division of Cardiovascular Surgery, Department of Surgery, Hsin Chu Armed Force Hospital, Hsinchu, Taiwan

7 Department of Internal Medicine, National Taiwan University Hospital, No. 7, Zhongshan S. Rd., Zhongzheng Dist., Taipei City, Taiwan 10002

References

1. Europe WHOROf: **Noncommunicable Diseases**. 2017.
2. DALYs GBD, Collaborators H: **Global, regional, and national disability-adjusted life-years (DALYs) for 359 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017**. *Lancet (London, England)* 2018, **392**(10159):1859-1922.
3. Agha G, Loucks EB, Tinker LF, Waring ME, Michaud DS, Foraker RE, Li W, Martin LW, Greenland P, Manson JE *et al*: **Healthy lifestyle and decreasing risk of heart failure in women: the Women's Health Initiative observational study**. *J Am Coll Cardiol* 2014, **64**(17):1777-1785. doi: 1710.1016/j.jacc.2014.1707.1981. Epub 2014 Oct 1721.
4. Ahmed HM, Blaha MJ, Nasir K, Jones SR, Rivera JJ, Agatston A, Blankstein R, Wong ND, Lakoski S, Budoff MJ *et al*: **Low-risk lifestyle, coronary calcium, cardiovascular events, and mortality: results from MESA**. *Am J Transplant* 2013, **13**(8):2191-2197. doi: 2110.1111/ajt.12274. Epub 12013 Jun 12274.
5. Akesson A, Larsson SC, Discacciati A, Wolk A: **Low-risk diet and lifestyle habits in the primary prevention of myocardial infarction in men: a population-based prospective cohort study**. *J Am Coll Cardiol* 2014, **64**(13):1299-1306. doi: 1210.1016/j.jacc.2014.1206.1190.

6. Åkesson A, Weismayer C, Newby PK, Wolk A: **Combined effect of low-risk dietary and lifestyle behaviors in primary prevention of myocardial infarction in women**. *Archives of Internal Medicine* 2007, **167**(19):2122-2127.
7. Cardi M, Munk N, Zanjani F, Kruger T, Schaie KW, Willis SL: **Health behavior risk factors across age as predictors of cardiovascular disease diagnosis**. *Arch Cardiovasc Dis* 2009, **102**(5):387-396. doi: 310.1016/j.acvd.2009.1002.1011. Epub 2009 Apr 1023.
8. Carlsson AC, Wändell PE, Gigante B, Leander K, Hellenius ML, De Faire U: **Seven modifiable lifestyle factors predict reduced risk for ischemic cardiovascular disease and all-cause mortality regardless of body mass index: A cohort study**. *International Journal of Cardiology* 2013, **168**(2):946-952.
9. Chomistek AK, Chiuve SE, Eliassen AH, Mukamal KJ, Willett WC, Rimm EB: **Healthy lifestyle in the primordial prevention of cardiovascular disease among young women**. *J Am Coll Cardiol* 2015, **65**(1):43-51. doi: 10.1016/j.jacc.2014.1010.1024.
10. Del Gobbo LC, Kalantarian S, Imamura F, Lemaitre R, Siscovick DS, Psaty BM, Mozaffarian D: **Contribution of Major Lifestyle Risk Factors for Incident Heart Failure in Older Adults: The Cardiovascular Health Study**. *JACC Heart Fail* 2015, **3**(7):520-528. doi: 510.1016/j.jchf.2015.1002.1009.
11. Díaz-Gutiérrez J, Ruiz-Canela M, Gea A, Fernández-Montero A, Martínez-González MÁ: **Association Between a Healthy Lifestyle Score and the Risk of Cardiovascular Disease in the SUN Cohort**. *Revista Espanola de Cardiologia* 2018, **71**(12):1001-1009.
12. Djoussé L, Driver JA, Gaziano JM: **Relation between modifiable lifestyle factors and lifetime risk of heart failure**. *JAMA - Journal of the American Medical Association* 2009, **302**(4):394-400.
13. Ford ES, Bergmann MM, Kröger J, Schienkiewitz A, Weikert C, Boeing H: **Healthy living is the best revenge: Findings from the European prospective investigation into cancer and nutrition-potsdam study**. *Archives of Internal Medicine* 2009, **169**(15):1355-1362.
14. Hoevenaar-Blom MP, Spijkerman AMW, Kromhout D, Verschuren WMM: **Sufficient sleep duration contributes to lower cardiovascular disease risk in addition to four traditional lifestyle factors: The MORGEN study**. *European Journal of Preventive Cardiology* 2014, **21**(11):1367-1375.
15. Hulsegge G, Looman M, Smit HA, Daviglus ML, van der Schouw YT, Verschuren WM: **Lifestyle Changes in Young Adulthood and Middle Age and Risk of Cardiovascular Disease and All-Cause Mortality: The Doetinchem Cohort Study**. *J Am Heart Assoc* 2016, **5(1).** (pii):JAHA.115.002432. doi: 002410.001161/JAHA.002115.002432.
16. Larsson SC, Åkesson A, Wolk A: **Healthy diet and lifestyle and risk of stroke in a prospective cohort of women**. *Neurology* 2014, **83**(19):1699-1704.
17. Larsson SC, Tektonidis TG, Gigante B, Akesson A, Wolk A: **Healthy Lifestyle and Risk of Heart Failure: Results From 2 Prospective Cohort Studies**. *Circulation Heart failure* 2016, **9**(4):e002855.
18. Lv J, Yu C, Guo Y, Bian Z, Yang L, Chen Y, Tang X, Zhang W, Qian Y, Huang Y *et al*: **Adherence to Healthy Lifestyle and Cardiovascular Diseases in the Chinese Population**. *J Am Coll Cardiol* 2017, **69**(9):1116-1125. doi: 1110.1016/j.jacc.2016.1111.1076.
19. Myint PK, Luben RN, Wareham NJ, Bingham SA, Khaw KT: **Combined effect of health behaviours and risk of first ever stroke in 20,040 men and women over 11 years' follow-up in Norfolk cohort of European Prospective Investigation of Cancer (EPIC Norfolk): prospective population study**. *Stroke* 2009, **40**(4):1070-1077. doi: 1010.1161/STROKEAHA.1108.533414. Epub 532009 Feb 533419.
20. Paynter NP, LaMonte MJ, Manson JE, Martin LW, Phillips LS, Ridker PM, Robinson JG, Cook NR: **Comparison of lifestyle-based and traditional cardiovascular disease prediction in a multiethnic cohort of nonsmoking women**. *Circulation* 2014, **130**(17):1466-1473. doi: 1410.1161/CIRCULATIONAHA.1114.012069. Epub 012014 Aug 012025.
21. Stampfer MJ, Hu FB, Manson JE, Rimm EB, Willett WC: **Primary prevention of coronary heart disease in women through diet and lifestyle**. *The New England journal of medicine* 2000, **343**(1):16-22.
22. Wang Y, Tuomilehto J, Jousilahti P, Antikainen R, Mahonen M, Katzmarzyk PT, Hu G: **Lifestyle factors in relation to heart failure among Finnish men and women**. *Diabet Med* 2012, **29**(3):393-398. doi: 310.1111/j.1464-5491.2011.03456.x.
23. Zhang Y, Tuomilehto J, Jousilahti P, Wang Y, Antikainen R, Hu G: **Lifestyle factors on the risks of ischemic and hemorrhagic stroke**. *Circ Heart Fail* 2011, **4**(5):607-612. doi: 610.1161/CIRCHEARTFAILURE.1111.962589. Epub 962011 Sep 962513.
24. Nyberg ST, Singh-Manoux A, Pentti J, Madsen IEH, Sabia S, Alfredsson L, Bjorner JB, Borritz M, Burr H, Goldberg M *et al*: **Association of Healthy Lifestyle With Years Lived Without Major Chronic Diseases**. *JAMA internal medicine* 2020, **180**(5):1-10.
25. Barbaresko J, Rienks J, Nöthlings U: **Lifestyle Indices and Cardiovascular Disease Risk: A Meta-analysis**. *American Journal of Preventive Medicine* 2018, **55**(4):555-564.
26. Research WCRFAIfC: **Second Expert Report on lifestyle recommendations**. 2007.
27. Bancks MP, Allen NB, Dubey P, Launer LJ, Lloyd-Jones DM, Reis JP, Sidney S, Yano Y, Schreiner PJ: **Cardiovascular health in young adulthood and structural brain MRI in midlife: The CARDIA study**. *Neurology* 2017, **89**(7):680-686.
28. Cao X, Zhou J, Yuan H, Chen Z: **Cumulative effect of reproductive factors on ideal cardiovascular health in postmenopausal women: a cross-sectional study in central south China**. *BMC cardiovascular disorders* 2015, **15**:176.

29. Folsom AR, Shah AM, Lutsey PL, Roetker NS, Alonso A, Avery CL, Miedema MD, Konety S, Chang PP, Solomon SD: **American Heart Association's Life's Simple 7: Avoiding Heart Failure and Preserving Cardiac Structure and Function**. *The American journal of medicine* 2015, **128**(9):970-976.e972.
30. Fretts AM, Howard BV, McKnight B, Duncan GE, Beresford SA, Mete M, Zhang Y, Siscovick DS: **Life's Simple 7 and incidence of diabetes among American Indians: the Strong Heart Family Study**. *Diabetes care* 2014, **37**(8):2240-2245.
31. Fretz A, McEvoy JW, Rebholz CM, Ndumele CE, Florido R, Hoogeveen RC, Ballantyne CM, Selvin E: **Relation of Lifestyle Factors and Life's Simple 7 Score to Temporal Reduction in Troponin Levels Measured by a High-Sensitivity Assay (from the Atherosclerosis Risk in Communities Study)**. *The American journal of cardiology* 2018, **121**(4):430-436.
32. Han L, You D, Ma W, Astell-Burt T, Feng X, Duan S, Qi L: **National Trends in American Heart Association Revised Life's Simple 7 Metrics Associated With Risk of Mortality Among US Adults**. *JAMA network open* 2019, **2**(10):e1913131.
33. Hernandez R, Gonzalez HM, Tarraf W, Moskowitz JT, Carnethon MR, Gallo LC, Penedo FJ, Isasi CR, Ruiz JM, Arguelles W *et al*: **Association of dispositional optimism with Life's Simple 7's Cardiovascular Health Index: results from the Hispanic Community Health Study/Study of Latinos (HCHS/SOL) Sociocultural Ancillary Study (SCAS)**. *BMJ open* 2018, **8**(3):e019434.
34. Samieri C, Perier MC, Gaye B, Proust-Lima C, Helmer C, Dartigues JF, Berr C, Tzourio C, Empana JP: **Association of Cardiovascular Health Level in Older Age With Cognitive Decline and Incident Dementia**. *Jama* 2018, **320**(7):657-664.
35. Ming-Chieh Tsai C-CL, Sung-Chen Liu, Po-Jung Tseng, Kuo-Liong Chien: **Healthy lifestyle habits are beneficial in reducing cardiovascular disease among young adults: A meta-analysis of prospective cohort studies**. *Scientific reports (revised)* 2020.
36. Wang WS, Wahlqvist ML, Hsu CC, Chang HY, Chang WC, Chen CC: **Age- and gender-specific population attributable risks of metabolic disorders on all-cause and cardiovascular mortality in Taiwan**. *BMC public health* 2012, **12**:111.
37. Su TC, Bai CH, Chang HY, You SL, Chien KL, Chen MF, Chen HJ, Pan WH, Tseng CH, Cheng SH *et al*: **Evidence for improved control of hypertension in Taiwan: 1993-2002**. *Journal of hypertension* 2008, **26**(3):600-606.
38. Hosmer DW Jr LS: **The multiple logistic regression model. Applied logistic regression. 1 ed.** 1989:25-37.
39. Hanley JA, McNeil BJ: **A method of comparing the areas under receiver operating characteristic curves derived from the same cases**. *Radiology* 1983, **148**(3):839-843.
40. DeLong ER, DeLong DM, Clarke-Pearson DL: **Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach**. *Biometrics* 1988, **44**(3):837-845.
41. Cook NR: **Use and misuse of the receiver operating characteristic curve in risk prediction**. *Circulation* 2007, **115**(7):928-935.
42. Pencina MJ, D'Agostino RB, Sr., D'Agostino RB, Jr., Vasan RS: **Evaluating the added predictive ability of a new marker: from area under the ROC curve to reclassification and beyond**. *Statistics in medicine* 2008, **27**(2):157-172; discussion 207-112.
43. Jankovic N, Geelen A, Winkels RM, Mwungura B, Fedirko V, Jenab M, Illner AK, Brenner H, Ordóñez-Mena JM, Kiefte de Jong JC *et al*: **Adherence to the WCRF/AICR Dietary Recommendations for Cancer Prevention and Risk of Cancer in Elderly from Europe and the United States: A Meta-Analysis within the CHANCES Project**. *Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology* 2017, **26**(1):136-144.
44. Barrubés L, Babio N, Hernández-Alonso P, Toledo E, Ramírez Sabio JB, Estruch R, Ros E, Fitó M, Alonso-Gómez AM, Fiol M *et al*: **Association between the 2018 WCRF/AICR and the Low-Risk Lifestyle Scores with Colorectal Cancer Risk in the Predimed Study**. *Journal of clinical medicine* 2020, **9**(4).
45. Hastert TA, White E: **Association between meeting the WCRF/AICR cancer prevention recommendations and colorectal cancer incidence: results from the VITAL cohort**. *Cancer causes & control : CCC* 2016, **27**(11):1347-1359.
46. Hastert TA, Beresford SA, Patterson RE, Kristal AR, White E: **Adherence to WCRF/AICR cancer prevention recommendations and risk of postmenopausal breast cancer**. *Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology* 2013, **22**(9):1498-1508.
47. Bruno E, Gargano G, Villarini A, Traina A, Johansson H, Mano MP, Santucci De Magistris M, Simeoni M, Consolaro E, Mercandino A *et al*: **Adherence to WCRF/AICR cancer prevention recommendations and metabolic syndrome in breast cancer patients**. *International journal of cancer* 2016, **138**(1):237-244.
48. Grafetstätter M, Pletsch-Borba L, Sookthai D, Karavasiloglou N, Johnson T, Katzke VA, Hoffmeister M, Bugert P, Kaaks R, Kühn T: **Thrombomodulin and Thrombopoietin, Two Biomarkers of Hemostasis, Are Positively Associated with Adherence to the World Cancer Research Fund/American Institute for Cancer Research Recommendations for Cancer Prevention in a Population-Based Cross-Sectional Study**. *Nutrients* 2019, **11**(9).
49. González HM, Tarraf W, Rodríguez CJ, Gallo LC, Sacco RL, Talavera GA, Heiss G, Kizer JR, Hernandez R, Davis S *et al*: **Cardiovascular health among diverse Hispanics/Latinos: Hispanic Community Health Study/Study of Latinos (HCHS/SOL) results**. *American heart journal* 2016, **176**:134-144.

50. Kim JY, Ko Y-J, Rhee CW, Park B-J, Kim D-H, Bae J-M, Shin M-H, Lee M-S, Li ZM, Ahn Y-O: **Cardiovascular Health Metrics and All-cause and Cardiovascular Disease Mortality Among Middle-aged Men in Korea: The Seoul Male Cohort Study**. *J Prev Med Public Health* 2013, **46**(6):319-328.
51. Miao C, Bao M, Xing A, Chen S, Wu Y, Cai J, Chen Y, Yang X: **Cardiovascular Health Score and the Risk of Cardiovascular Diseases**. *PloS one* 2015, **10**(7):e0131537.
52. Folsom AR, Yatsuya H, Nettleton JA, Lutsey PL, Cushman M, Rosamond WD: **Community Prevalence of Ideal Cardiovascular Health, by the American Heart Association Definition, and Relationship With Cardiovascular Disease Incidence**. *J Am Coll Cardiol* 2011, **57**(16):1690-1696.
53. Ford ES, Greenlund KJ, Hong Y: **Ideal cardiovascular health and mortality from all causes and diseases of the circulatory system among adults in the United States**. *Circulation* 2012, **125**(8):987-995.
54. Artero EG, España-Romero V, Lee D-c, Sui X, Church TS, Lavie CJ, Blair SN: **Ideal Cardiovascular Health and Mortality: Aerobics Center Longitudinal Study**. *Mayo Clinic proceedings* 2012, **87**(10):944-952.
55. Lachman S, Peters RJG, Lentjes MAH, Mulligan AA, Luben RN, Wareham NJ, Khaw K-T, Boekholdt SM: **Ideal cardiovascular health and risk of cardiovascular events in the EPIC-Norfolk prospective population study**. *European Journal of Preventive Cardiology* 2015, **23**(9):986-994.
56. Liu Y, Chi H-j, Cui L-f, Yang X-c, Wu Y-t, Huang Z, Zhao H-y, Gao J-s, Wu S-l, Cai J: **The Ideal Cardiovascular Health Metrics Associated Inversely with Mortality from All Causes and from Cardiovascular Diseases among Adults in a Northern Chinese Industrial City**. *PloS one* 2014, **9**(2):e89161.
57. Dong C, Rundek T, Wright CB, Anwar Z, Elkind MS, Sacco RL: **Ideal cardiovascular health predicts lower risks of myocardial infarction, stroke, and vascular death across whites, blacks, and hispanics: the northern Manhattan study**. *Circulation* 2012, **125**(24):2975-2984.
58. Kulshreshtha A, Vaccarino V, Judd SE, Howard VJ, McClellan WM, Muntner P, Hong Y, Safford MM, Goyal A, Cushman M: **Life's Simple 7 and risk of incident stroke: the reasons for geographic and racial differences in stroke study**. *Stroke* 2013, **44**(7):1909-1914.
59. Karmali KN, Goff DC, Jr., Ning H, Lloyd-Jones DM: **A systematic examination of the 2013 ACC/AHA pooled cohort risk assessment tool for atherosclerotic cardiovascular disease**. *J Am Coll Cardiol* 2014, **64**(10):959-968.
60. Bress AP, Colantonio LD, Booth JN, 3rd, Spruill TM, Ravenell J, Butler M, Shallcross AJ, Seals SR, Reynolds K, Ogedegbe G *et al*: **Modifiable Risk Factors Versus Age on Developing High Predicted Cardiovascular Disease Risk in Blacks**. *Journal of the American Heart Association* 2017, **6**(2).
61. Shirakawa K, Endo J, Katsumata Y, Yamamoto T, Kataoka M, Isobe S, Yoshida N, Fukuda K, Sano M: **Negative legacy of obesity**. *PloS one* 2017, **12**(10):e0186303.

Tables

Table 1: Basic characteristics of the study participants at baseline, specified by adherence numbers of healthy lifestyle scores according to the simple Taiwan healthy lifestyle score (0~5 points)

	Whole population		Simple Taiwan Healthy Lifestyle Score				
The numbers of score	(n= 6048)		0~1(n=1332)	2 (n=2438)	3 (n=1811)	4~5 (n=461)	*P*
	%						
Women	50.2		28.2	53.3	59.3	62	<.001
Age (years) 20-39	41.1		30.3	35.5	51.1	62.5	<.001
40-59	39.2		44.1	41.4	34.7	31	
≧60	19.7		25.6	23.2	14.2	6.5	
Body mass index (kg/m^2) < 25	73.2		31.38	75.88	94.76		<.001
≧25	26.9		68.62	24.12	5.24		
Mediterranean diet score ≧6	47.2		12.84	33.96	81.47		<.001
< 6	52.8		87.16	66.04	18.53		
Exercise time 1~150 mins/week	23		3.2	11.4	34.5	96.1	<.001
0 or >150 mins/week	77		96.8	88.6	65.5	3.9	
Never smoking	71.3		34.2	73	89.8	97	<.001
Quit and current smoking	28.7		65.8	27	10.2	3	
Adeaute drinking	5.1		2.4	5.7	5.4	8.7	<.001
Non or few drinking	94.9		97.6	94.3	94.6	91.3	
Marital status: Living with spouse	64.6		29.1	33.3	40.5	44.7	<.001
Single, divorced or separated	35.4		71	66.7	59.5	55.3	
Education level: ≦9 years	45.7		58.6	51	35.1	22.1	<.001
> 9 years	54.3		41.4	49	64.9	77.9	
Monthly income < 40000 NTD	79.6		79.2	81.9	78.1	74.8	0.001
≧ 40000 NTD	20.4		20.8	18.1	21.9	25.2	
Parents history of CVD	21.9		24.5	22.4	20.8	16.9	0.004
Menopause status	17.3		16	21.9	14.6	7.4	<.001
Hypertension	15.7		24.9	17.1	9.8	5.4	<.001
Diabetes Mellitus	4.4		7.4	4.6	2.8	0.7	<.001
History of hyperlipidemia	7.2		9.3	7.6	5.9	4.3	<.001
HRT use	8		6.5	8.7	8.2	7.6	0.125
Variable	Mean	SD	Mean				*P*
Systolic BP, mmHg	116.5	18.2	122.1	118	112.6	107.7	<.001
Diastolic BP, mmHg	75.6	11.4	79.6	75.9	73.3	70.9	<.001
Total cholesterol, mg/dL	186.1	37.9	191.3	187.2	182.6	178.7	<.001
Triglyceride, mg/dL	130.1	86.6	163.6	129.5	112.8	105.2	<.001
HDL-cholesterol, mg/dL	55.5	15.3	51.3	55.9	57.5	57.9	<.001
LDL-cholesterol, mg/dL	117.1	27.2	121.2	118.4	113.9	110.6	<.001
Non-HDL-cholesterol, mg/dL	130.6	35.3	140	131.3	125.2	120.8	<.001
Fasting glucose, mg/dL	95	29.4	101.1	95.5	91.8	87.1	<.001
Hemoglobin A1c, %	5.4	1.1	5.6	5.4	5.2	5.1	<.001

Abbreviation: SD, standard deviation; BP, blood pressure; HDL, high density lipoprotein, LDL, low density lipoprotein; ANOVA and the chi-square tests were used to compare the means and proportions among groups

Table 2: The incidence cases, follow-up person-years, and the rates of cardiovascular disease events according to lifestyle factors and the hazard ratios and 95% confidence intervals specified by The simple Taiwan healthy lifestyle score, according to the numbers of the score

	0~1	2			3			4~5			*P* of Logrank			
Cases	193	228			87			12						
Pearson-year	15840.3	30091.5			23459.7			6163.6						
Rates/1000 py	12.18	7.6			3.71			1.95			< 0.001			
	HR	HR	95% CI		HR	95% CI		HR	95% CI		*P* of Trend Test	PAF	95% CI	
Univariate	1.00	0.56	0.45	0.69	0.26	0.20	0.35	0.14	0.07	0.27	< 0.001			
Model 1	1.00	0.72	0.58	0.90	0.48	0.35	0.64	0.37	0.19	0.72	< 0.001			
Model 2	1.00	0.75	0.60	0.94	0.53	0.39	0.71	0.42	0.21	0.82	< 0.001			
Model 3	1.00	0.77	0.60	0.99	0.53	0.38	0.74	0.43	0.20	0.94	< 0.001	38.8	19.2	53.6

(Note: Model 1: adjusted for age and sex; Model 2: Model 1, additionally education, average month income, marital status, parental history of CVD, menopause status and estrogen exposure; Model 3: Model 2 + baseline HTN, baseline DM, history of hyperlipidemia, sBP, dBP, triglyceride, non-HDL, fasting glucose, HbA1c; The population attributable risk is the percentage of new cases of heart failure in the population attributable to nonadherence to the low-risk lifestyle factor.)

Table 3: Hazard ratios for cardiovascular disease among participants stratified by age < 60 y/o and ≥ 60 y/o, specified by simple Taiwan healthy lifestyle score, weighted Taiwan healthy lifestyle score, WCRF/AICR recommended healthy lifestyle and Life's Simple 7 according to the numbers of healthy lifestyle factors

		Group 1	Group 2			Group 3			Group 4			
		HR	HR	95% CI		HR	95% CI		HR	95% CI		$P_{interaction}$
MDS	age < 60	1	0.65	0.44	0.96	0.37	0.21	0.63	0.35	0.13	0.99	0.070
	age ≥ 60	1	0.88	0.64	1.22	0.67	0.44	1.03	0.56	0.17	1.79	
Taiwan	age < 60	1	0.60	0.37	0.96	0.53	0.32	0.88	0.31	0.15	0.61	0.029
	age ≥ 60	1	0.96	0.66	1.41	0.81	0.54	1.21	0.60	0.33	1.07	
WCRF	age < 60	1	0.86	0.45	1.64	0.84	0.44	1.59	1.30	0.67	2.51	0.011
	age ≥ 60	1	3.26	0.77	13.84	2.95	0.71	12.26	2.65	0.64	11.04	
LS7	age < 60	1	1.25	0.59	2.63	0.61	1.24	0.54	0.97	0.32	2.98	0.234
	age ≥ 60	1	0.62	0.31	1.23	0.26	0.66	0.32	0.45	0.17	1.18	

Note: Group1 as those with lowest number of healthy lifestyle score, Group 2 and Group 4 as those with increasing the numbers of healthy lifestyle score

Table 4: Improvement in discrimination performance and calibration for risk prediction of cardiovascular events in the multivariate-adjusted model after including Mediterranean diet related healthy lifestyle score, Taiwan healthy lifestyle score, WCRF/AICR recommendation lifestyle and Life's Simple 7

	AUC	95% CI		P	P for HL test	IDI (%)	95% CI		P	NRI (%)	95% CI		P
Clssical model	0.85	0.837	0.870	Reference									
Simple Taiwan	0.86	0.842	0.874	0.02	0.34	0.38	0.01	0.74	0.021	0.03	0.01	0.05	0.004
Weighted Taiwan	0.86	0.840	0.873	0.003	0.25	0.51	0.16	0.86	0.002	0.04	0.02	0.06	<.001
WCRF/AICR	0.85	0.838	0.870	0.49	0.49	0.10	-0.03	0.24	0.07	0.07	-1.15	1.29	0.91
Life's Simple 7	0.85	0.837	0.870	0.80	0.73	0.09	-0.06	0.24	0.11	0.95	-0.37	2.28	0.16

Note: CVD risk classification (0,0.01,0.05,0.1)

Supplement

Figures

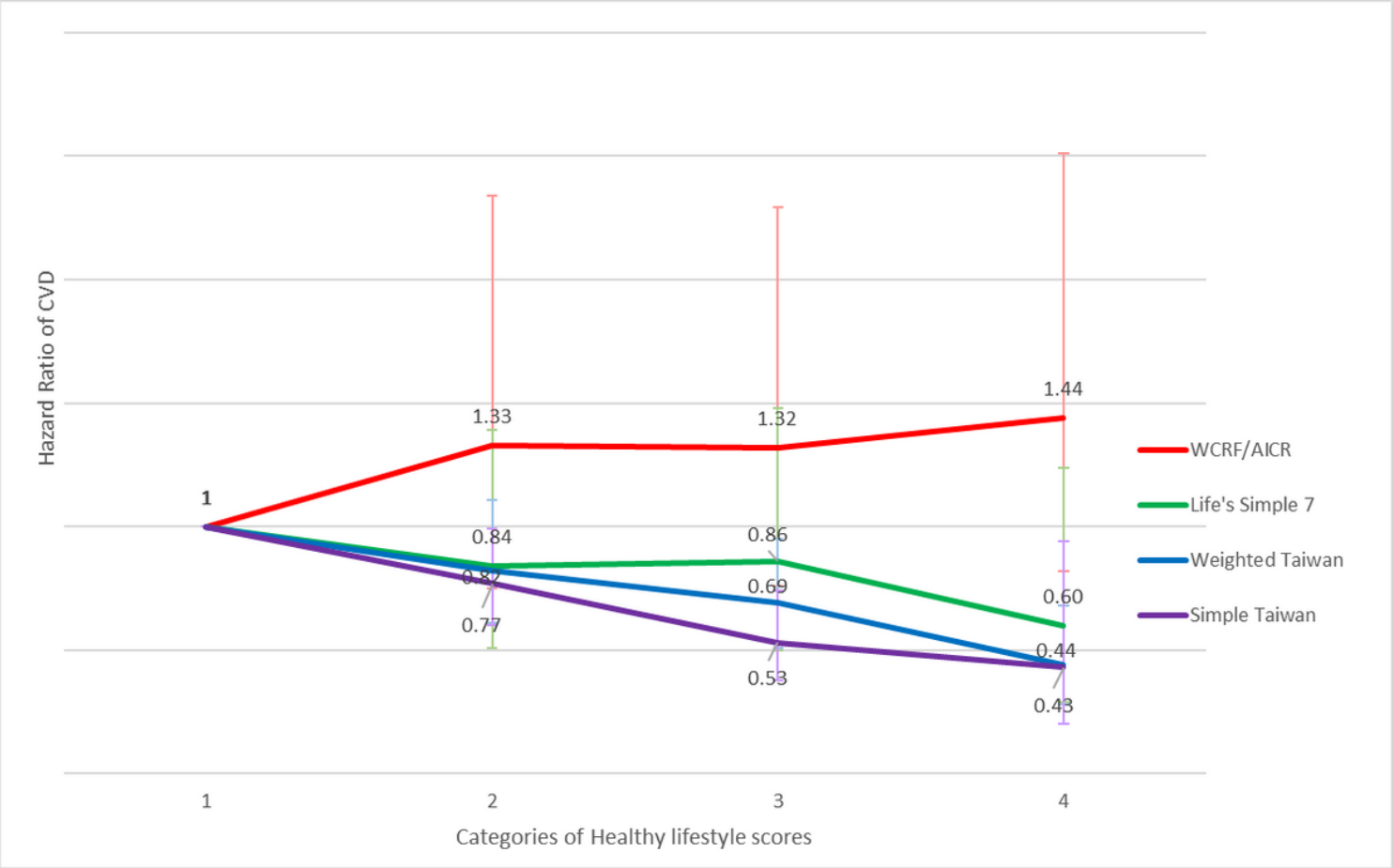

Figure 1

Hazard ratios for cardiovascular disease specified by categories according to the numbers of healthy lifestyle factors among participants stratified by simple Taiwan healthy lifestyle score, weighted Taiwan healthy lifestyle score, WCRF/AICR recommended healthy lifestyle score and Life's Simple 7

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- TablefigureandsupplementCD.20200915.docx