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

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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, 0.87; 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 (drinking 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
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 (Pdiff=0.02) for the simple Taiwan healthy lifestyle score and significantly increased from 0.84 to 0.87 (Pdiff=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 Health Insurance 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.

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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)
| Variable                                      | Whole population | Simple Taiwan Healthy Lifestyle Score |
|-----------------------------------------------|------------------|----------------------------------------|
|                                               | (n= 6048)        | 0~1 (n=1332) 2 (n=2438) 3 (n=1811) 4~5 (n=461) |
| The numbers of score                          | %                | %                                      |
| 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 <.001                |
| ≥60                                           | 19.7             | 25.6 23.2 14.2 6.5 <.001               |
| Body mass index (kg/m²) < 25                  | 73.2             | 31.38 75.88 94.76 <.001                |
| ≥25                                           | 26.9             | 68.62 24.12 5.24 <.001                 |
| Mediterranean diet score ≥6                   | 47.2             | 12.84 33.96 81.47 <.001                |
| < 6                                           | 52.8             | 87.16 66.04 18.53 <.001                |
| 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 <.001               |
| Never smoking                                 | 71.3             | 34.2 73 89.8 97 <.001                  |
| Quit and current smoking                      | 28.7             | 65.8 27 10.2 3 <.001                   |
| Adequate 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 SD 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   |

(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 | 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: Group 1 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   |
|----------------|------|--------|-------|--------------|---------|--------|-------|---------|--------|-----|
| Classical 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 |
|                |      |        |       |              |         |        |       |         |        |     |
| Weighted Taiwan| 0.86 | 0.840  | 0.873 | 0.003        | 0.25    | 0.51   | 0.16  | 0.86    | 0.002  | 0.04 |
|                |      |        |       |              |         |        |       |         |        |     |
| WCRF/AICR      | 0.85 | 0.838  | 0.870 | 0.49         | 0.49    | 0.10   | -0.03 | 0.24    | 0.07   | 0.07 |
|                |      |        |       |              |         |        |       |         |        |     |
| Life’s Simple 7| 0.85 | 0.837  | 0.870 | 0.80         | 0.73    | 0.09   | -0.06 | 0.24    | 0.11   | 0.95 |

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

Supplement

Protocol of healthy lifestyle scores for the risk of cardiovascular diseases

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