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Higher Healthy Lifestyle Score is associated with lower presence of non-alcoholic fatty liver disease in middle-aged and older Chinese adults: a community-based cross-sectional study

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Abstract

Objective: Previous studies have reported inverse associations between certain healthy lifestyle factors and non-alcoholic fatty liver disease (NAFLD), but limited evidence showed the synergistic effect of those lifestyles. This study examined the relationship of a combination of lifestyles, expressed as Healthy Lifestyle Score (HLS), with NAFLD.

Design: A community-based cross-sectional study. Questionnaires and body assessments were used to collect data on the six-item HLS (ranging from 0 to 6, where higher scores indicate better health). The HLS consists of non-smoking (no active or passive smoking), normal BMI (18·5–23·9 kg/m^2), physical activity (moderate or vigorous physical activity ≥ 150 min/week), healthy diet pattern, good sleep (no insomnia or <6 months) and no anxiety (Self-rating Anxiety Scale < 50), one point each. NAFLD was diagnosed by ultrasonography.

Setting: Guangzhou, China.

Participants: Two thousand nine hundred and eighty-one participants aged 40–75 years.

Results: The overall prevalence of NAFLD was 50·8 %. After adjusting for potential covariates, HLS was associated with lower presence of NAFLD. The OR of NAFLD for subjects with higher HLS (3, 4, 5–6 *v.* 0–1 points) were 0·68 (95 % CI 0·51, 0·91), 0·58 (95 % CI 0·43, 0·78) and 0·35 (95 % CI 0·25, 0·51), respectively (*P*-values < 0·05). Among the six items, BMI and physical activity were the strongest contributors. Sensitivity analyses showed that the association was more significant after weighting the HLS. The beneficial association remained after excluding any one of the six components or replacing BMI with waist circumference.

Conclusions: Higher HLS was associated with lower presence of NAFLD, suggesting that a healthy lifestyle pattern might be beneficial to liver health.

Keywords
Lifestyle
Healthy Lifestyle Score
Fatty liver disease
Liver health
Chinese

Non-alcoholic fatty liver disease (NAFLD) is one of the most important liver diseases which involves simple fatty infiltration (steatosis), fatty infiltration plus inflammation (NASH), fibrosis and ultimately cirrhosis, without excessive alcohol consumption[1]. The prevalence of NAFLD was about 17 %–46 % around the world with diagnosis of liver ultrasound[2] and 12·5 %–27·3 % in the general population of China[3]. This disease has brought a huge health burden globally[1]. Therefore, effective public health measures should be implemented.

A large number of studies have shown that lifestyle factors play key roles in the prevention and treatment of NAFLD, such as non-smoking[4], moderate physical activity[5], a healthy diet[6,7], normal body weight[8], moderate sleep duration[9] and low anxiety level[10]. However, most of these studies only explored the association between individual lifestyle factors and NAFLD, thus ignoring the fact that each specific healthy lifestyle factor was capable

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Public Health Nutrition

of coexisting with the others and may result in a synergistic effect on people's health[11]. Therefore, establishing a combined measure of these relevant lifestyle components, such as the Healthy Lifestyle Score (HLS), may be more useful in evaluating synergistic associations than using each single lifestyle behaviour.

Many studies showed that the HLS is associated with CVD[12–14], some cancers[15–17], osteoporosis[18] and other diseases[19]. In these studies, HLS normally consisted of the following lifestyles: smoking, body weight or BMI, physical activity, diet, sleep, anxiety, etc. To our knowledge, only one study has explored the association between the healthy lifestyle index (HLI) and fatty liver disease (FLD) among 354 Germans (mean age 67·1 years)[20]. In that study, individuals with all four (*v.* zero) favourable lifestyle factors (never smoking, favourable waist circumference (WC), moderate physical activity and healthy diet) had lower OR values for FLD (0·09; 95 % CI 0·03, 0·30).

However, there are two problems with using the HLI to assess the risk of NAFLD. First, the components of the HLI may be inappropriate. For example, the diet component included alcohol consumption, a key determinant of liver diseases. A study of 653 Chinese individuals showed that alcohol intake ≥20 g/d and drinking duration ≥5 years were associated with greater odds of liver injury (OR: 1·96 (95 % CI 1·12, 3·44) and 3·41 (95 % CI 1·79, 6·51), respectively, $P < 0·05$)[21]. In addition, the HLI did not include other lifestyle factors related to NAFLD, such as passive smoking[4], BMI[8], sleep[9] and anxiety[10]. Second, each individual component was treated equally and had the same weight not only in that study but also in many other HLS-related studies, thus ignoring the fact that the strengths of the associations may differ for the different component lifestyle factors[16,22].

To address these issues, this cross-sectional study examined the association of a six-item HLS (non-smoking, normal BMI, physically active, healthy diet pattern, good sleep and no anxiety) with NAFLD in a middle-aged and older Chinese population and explored the optimal weight for each item based on a regression model.

Methods

Study participants

This study was based on the Guangzhou Nutrition and Health Study (GNHS), which is a community-based prospective cohort study designed to assess determinants of common chronic diseases (e.g. osteoporosis, NAFLD, cardiometabolic diseases). Participants (aged 40–75 years old) who had lived in urban Guangzhou for ≥5 years were recruited from 2008 to 2010 (*n* 3169) and 2012 to 2013 (*n* 879) using the same criteria. Questionnaire interviews, body assessments and ultrasonography evaluations for NAFLD were conducted among 3389 participants who completed the survey between 2011 and 2013, including 2510 subjects from the first batch and 879 newly recruited subjects. A total of 408 participants were excluded from this study for the following reasons: (1) history of malignancy, hyperthyroidism or viral hepatitis (*n* 98); (2) excessive alcohol consumption (*n* 24): ≥30 g/d (men) or ≥20 g/d (women)[1]; (3) missing data to calculate HLS or to determine the status of NAFLD (*n* 219) and (4) extreme energy intake (*n* 67): <3348 or >17 581 kJ/d (men); <2512 or >14 650 kJ/d (women). Finally, 2981 participants were included in this study (Figure 1).

Definition and assessment of the Healthy Lifestyle Score

The HLS in this study consists of six components: non-smoking, normal BMI, physical activity, healthy diet pattern, good sleep and no anxiety. One point was awarded for a healthy status and 0 point for an unhealthy status with respect to each item (Table 1), with a maximum score of six points (higher scores indicate better health). Face-to-face interviews using structured questionnaires[23] and body assessments were used to collect HLS-relevant information and covariates, such as age, sex, marital status, education level, income, history of diseases and drugs (such as statins), and use of oral oestrogen. Smoking included both active (cigarette consumption ≥100 in the last year) and passive smoking (cigarette exposure ≥1/d in the last year). Physical activity referred to moderate or vigorous activity[24]. Participants' heights and weights were measured to calculate BMI (in kg/m^2). WC was measured at the widest part of the stomach (across the belly button, just above the hipbones) when participants were standing and just after breathing out. WC below 85 cm (men) or 80 cm (women) was classified as healthy[25]. The alternate Mediterranean diet score[26,27] was used to assess the diet. We further modified it by excluding alcohol intake since it was a typical risk factor for liver diseases[21]. The modified alternate Mediterranean diet score ranged from 0 to 8 (higher scores indicate better health) and included eight dietary components: whole grains, vegetables (excluding potatoes), fruit (including juices), legumes, nuts, fish, ratio of MUFA to SFA and red or processed meats. Insomnia was defined as having any of the following conditions for more than 6 months prior to the survey: (1) cannot get to sleep within 30 min; (2) wake up early or in the middle of the night and (3) actual sleep time <7 h/night. Anxiety neurosis was assessed using a twenty-item Self-rating Anxiety Scale[28]. Each item was given a four-grade score (1–4 points) to assess the frequency of anxiety symptoms. A full standard score of 100 points was then obtained by adding the scores of twenty items and multiplying by 1·25. Participants were classified as normal, mild, moderate and severe anxiety neurosis according to the standard score of <50, 50–59, 60–69 and ≥70, respectively.

Assessment of non-alcoholic fatty liver disease

NAFLD was evaluated by using abdominal ultrasonography (Doppler sonography machine, Sonoscape SSI-5500)

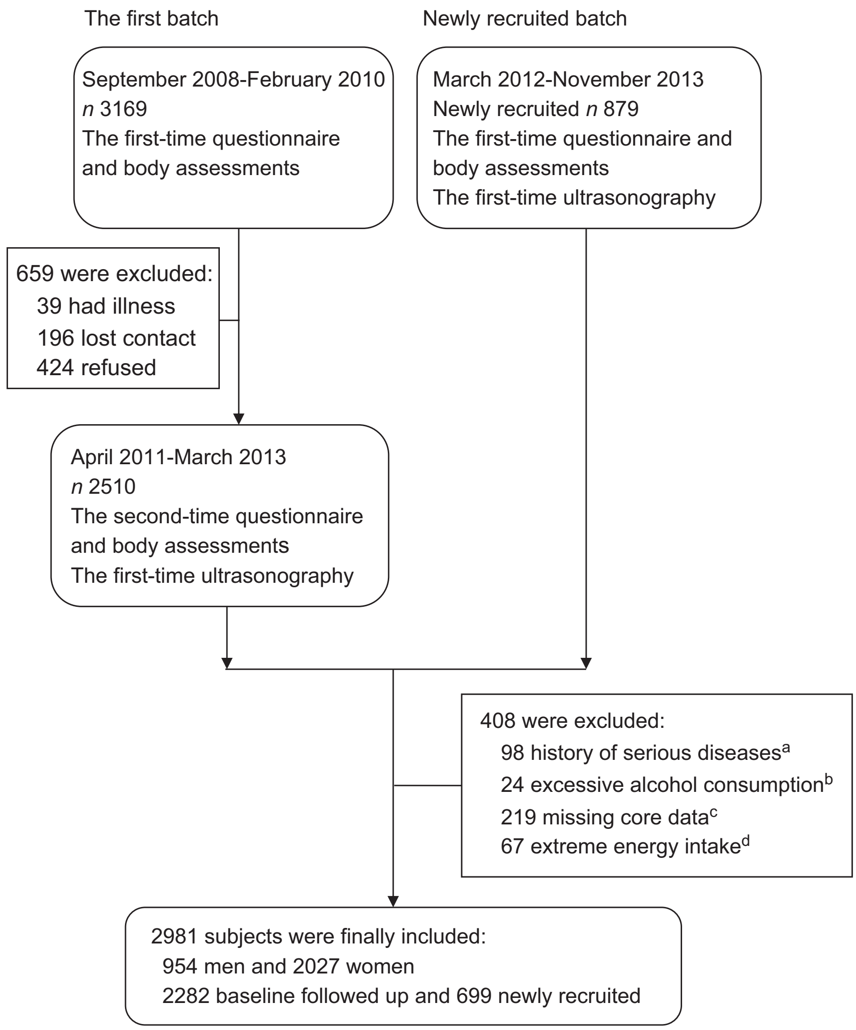

Fig. 1 (colour online) The flow chart of participants in the present study. (a) Serious diseases: malignancy, hyperthyroidism or viral hepatitis. (b) Excessive alcohol consumption: ≥30 g/d (men) or ≥20 g/d (women). (c) Core data: data to calculate the Healthy Lifestyle Score or to determine the status of non-alcoholic fatty liver disease. (d) Extreme energy intake: <3348 or >17 581 kJ/d (men); <2512 or >14 650 kJ/d (women)

according to Graif's criteria[29], in which radiologists were blinded to the participants' information. The reliability was evaluated by repeatedly testing 100 participants, and the results showed great reliability ($\kappa = 0{\cdot}875$, total agreement = 93 %, $P < 0{\cdot}001$). The validity was assessed in thirty-four participants using computed tomography by researchers who did not know the ultrasonography results, and the results indicated good validity ($\kappa = 0{\cdot}691$, total agreement = 85 %, $P < 0{\cdot}001$).

Statistical analysis

Baseline data were presented as the mean and standard deviation (SD) for continuous variables, and frequency and percentage for categorical variables. All continuous variables followed a normal distribution assessed by the Q-Q plot. ANOVA and the χ^2 test were used to compare differences in baseline data among the five HLS groups as appropriate (we combined HLS groups when the sample size was too small).

Logistic regression was used to estimate OR of NAFLD under two models in all subjects, men and women. Only age and sex were adjusted in model 1. In model 2, marital status, education level, income, history of using statins and daily energy intake were further adjusted. For women, we further adjusted for menopausal age and oral oestrogen use. The statistical power of the logistic model (model 2) was estimated for the calculation of OR by treating HLS as a continuous variable. We also explored the association of each component of HLS with NAFLD by logistic regression under the same two models, and other components of HLS except the one being analysed were further adjusted in model 2.

The sensitivity analyses included the following. (1) Comparison of HLS and weighted HLS (wHLS): a wHLS was calculated based on the standardised β ($s\beta$) values of the six components ($\text{weight}_i = [s\beta_i/(\Sigma s\beta_i)] \times 6$); wHLS

Table 1 Criteria of Healthy Lifestyle Score in the present study

Lifestyle factors	Score
Smoking	
No active or passive smoking	1
Currently active or passive smoking	0
BMI	
$18.5 \leq$ BMI < 24.0 kg/m^2	1
BMI < 18.5 or ≥ 24.0 kg/m^2	0
Physical activity	
Moderate or vigorous physical activity ≥ 150 min/week	1
Moderate or vigorous physical activity < 150 min/week	0
Diet	
Modified alternate Mediterranean diet score: 5–8	1
Modified alternate Mediterranean diet score: 0–4	0
Sleep	
Did not have insomnia or <6 months	1
Have insomnia ≥6 months	0
Anxiety	
Self-Rating Anxiety Scale (SAS) < 50	1
SAS ≥ 50	0

was divided into five groups, and the sample size of each group was similar to that of HLS. (2) The stability of the HLS was assessed by excluding each component of HLS in turn and replacing the BMI with WC. (3) The synergy of weaker factors: we calculated HLS weaker factors, which consisted of components that showed little or no association with NAFLD in individual lifestyle factor analysis. SPSS 22.0 (IBM) and PASS 11.0 (NCSS, LLC.) were used to perform the statistical analyses, and a two-sided *P*-value <0·05 was considered statistically significant in this study.

Results

A total of 2981 subjects (954 men and 2027 women) were included in this study. The mean ages of all subjects, men and women were 60·6, 62·2 and 59·9 years old, respectively, and the prevalence of NAFLD was 50·8 %, 54·0 % and 49·3 %, respectively. With the increase in HLS, participants had higher levels of income, education, physical activity, energy intake, dietary intakes of whole grain, vegetables, fruits, legumes, nuts and fish, and adherence to the modified alternate Mediterranean diet score. For women, menopausal age and the proportion of oestrogen use also increased. In contrast, as HLS increased, subjects had lower levels of body weight and BMI and fewer proportions of current smoking, insomnia and anxiety (all *P*-values < 0·05) (Table 2).

In all subjects (Table 3), higher HLS was inversely associated with NAFLD after adjusting for age and sex in model 1. The OR of NAFLD for subjects with higher HLS (3, 4, 5–6 *v.* 0–1 points) were 0·68 (95 % CI 0·51, 0·91), 0·58 (95 % CI 0·43, 0·79) and 0·37 (95 % CI 0·26, 0·52), respectively (all *P*-values < 0·05). The same trends were observed in model 2, with corresponding OR of 0·68 (95 % CI 0·51, 0·91), 0·58 (95 % CI 0·43, 0·78) and 0·35 (95 % CI 0·25, 0·51), respectively (all *P*-values < 0·05), with a power of almost 100 % at a 0·05 significance level. In the sex-stratified analysis, the inverse association was only found in women, in which the corresponding OR (model 2) of NAFLD for subjects with higher HLS (3, 4, 5–6, *v.* 0–1 points) were 0·51 (95 % CI 0·34, 0·77), 0·44 (95 % CI 0·28, 0·67) and 0·25 (95 % CI 0·15, 0·41), respectively (Table 3). Among the six individual components of HLS, only normal BMI (OR 0·30) and physical activity (OR 0·81) were significantly associated with a lower likelihood of NAFLD in model 2 (*P*-values < 0·05) (Table 4).

Weighted HLS was calculated according to the standardised regression beta for each individual item with NAFLD. BMI and physical activity contributed most to the wHLS with weights of 3·94 and 0·73, and the weights of the other four items ranged from 0·15 (anxiety) to 0·52 (insomnia) (online Supplementary Table 1). The associations of wHLS with the presence of NAFLD tended to be stronger than those of HLS. The OR of NAFLD were 0·37, 0·30 and 0·23 for the higher wHLS groups (3, 4, 5 *v.* 1 points) in model 2 (all *P*-values < 0·001). The sensitivity analyses showed that the beneficial associations between HLS and NAFLD remained after excluding each component in turn, excluding the two most significant factors (BMI and physical activity), or replacing BMI with WC (*P*-values < 0·05) (online Supplementary table 2).

Discussion

The six-item HLS was inversely associated with NAFLD in this middle-aged and older Chinese population. BMI and physical activity were two key contributors to the association. The OR for NAFLD of weighted HLS were lower than those of HLS consisting of equal weight components. These results suggested that subjects with better adherence to a healthy lifestyle pattern (non-smoking, normal BMI, physically active, a healthy diet, good sleep and no anxiety) might have a lower risk of NAFLD, and a high weighted HLS may lead to more benefits than a high unweighted HLS.

Healthy Lifestyle Score and non-alcoholic fatty liver disease

Previous studies have explored the relationship between individual lifestyle factors and NAFLD[4–10]; however, few studies have reported associations between synergistic lifestyle scores and NAFLD. To the best of our knowledge, only one cross-sectional study (including 354 Germans aged 67·1 years old) has examined the association of the HLI with FLD.[20] The HLI consisted of smoking, WC, physical activity and diet and ranged from 0 to 4 points (higher scores indicate better health). Consistent with our results, the study suggested an inverse association between HLI and FLD. The OR of FLD for subjects who had high HLI (2, 3 and 4 points) were 0·35 (95 % CI 0·16–0·80), 0·25 (95 % CI 0·10–0·61) and 0·09 (95 % CI 0·03–0·30), respectively.

Table 2 Baseline characteristics of study participants by Healthy Lifestyle Score (HLS)*

	HLS ($n = 2981$)										
	0–1		2		3		4		5–6		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	*P*-value
n	238		718		984		753		288		
%	8.0		24.1		33.0		25.2		9.7		
Sex											<0.001
Men ($n = 954$)											
n	36		235		342		235		106		
%	15.1		32.7		34.8		31.2		36.8		
Age (years)	60.4	6.2	60.8	6.0	60.8	6.1	60.4	5.5	60.3	5.3	0.375
Body weight (kg)	59.3	8.2	60.1	9.6	59.4	9.9	58.3	9.5	58.1	9.0	0.002
BMI (kg/m^2)	24.8	2.9	24.2	3.0	23.5	3.0	22.8	2.7	22.1	2.3	<0.001
Waist circumference (cm)	87.5	9.0	86.4	8.4	84.6	8.5	83.2	8.1	81.6	7.4	0.062
Household income											<0.001
<2000 Yuan/month per person	60	25.2	127	17.7	151	15.3	110	14.6	43	14.9	
2000–3000 Yuan/month per person	100	42.0	255	35.5	416	42.3	299	39.7	111	38.5	
>3000 Yuan/month per person	78	32.8	336	46.8	417	42.4	344	45.7	134	46.5	
Education (years)											<0.001
<9	101	42.4	232	32.3	259	26.3	165	21.9	50	17.4	
9–12	107	45.0	346	48.2	465	47.3	371	49.3	150	52.1	
>12	30	12.6	140	19.5	260	26.4	217	28.8	88	30.6	
Married	202	84.9	643	89.6	874	88.8	665	88.3	253	87.8	0.394
History of using statins	40	16.8	105	14.6	116	11.8	85	11.3	35	12.2	0.087
Smoker†	169	71.0	394	54.9	292	29.7	96	12.7	0	0.0	<0.001
Physical activity‡ (min/week)	52.8	125	105	200	201	251	321	261	449	246	<0.001
Energy intake (kcal/d)	1430	390	1523	425	1585	466	1660	461	1799	479	<0.001
Components of modified aMed score											
Whole grains§ (g/d)	2.9	3.2	4.76	13.9	5.2	13.1	5.4	5.9	6.51	5.6	0.003
Vegetables (excluded potatoes) (g/d)	22.9	9.1	24.8	10.8	26.8	11.8	30.7	12.1	34.8	13.7	<0.001
Fruits (included juices) (g/d)	17.2	11.0	19.2	18.6	21.7	29.1	25.5	14.0	29.2	14.1	<0.001
Legumes‖ (g/d)	3.7	4.3	4.0	4.1	5.2	6.6	5.7	5.9	7.1	5.7	<0.001
Nuts (g/d)	2.4	5.8	2.4	3.1	2.9	3.9	3.8	3.9	5.1	4.6	<0.001
Fish (g/d)	10.7	22.1	10.5	7.6	12.2	19.1	13.2	10.3	16.2	12.3	<0.001
MUFA/SFA	1.4	0.2	1.4	0.2	1.4	0.2	1.4	0.2	1.4	0.2	0.808
Red and processed meats (g/d)	30.1	25.5	29.9	16.8	30.3	16.4	29.8	19.5	28.9	16.7	0.668
High adherence of modified aMed score	17	7.1	104	14.5	324	32.9	488	64.8	288	100.0	<0.001
Insomnia¶	69	29.0	59	8.2	39	4.0	11	1.5	0	0.0	<0.001
Anxiety neurosis**	116	48.7	104	14.5	69	7.0	14	1.9	0	0.0	<0.001
Ultrasound-based NAFLD	142	59.7	409	57.0	505	51.3	355	47.1	104	36.1	<0.001
Women											
Menopause age (years)	46.5	12.6	48.9	8.1	48.7	8.7	48.7	8.6	48.9	9.1	0.005
Oestrogen user	10	5.2	20	4.3	45	7.2	38	7.5	20	10.5	0.035

Modified aMed score, modified alternate Mediterranean diet score; NAFLD, non-alcoholic fatty liver disease.
*Continuous variables were presented as mean and SD, while categorical variables as frequency and percentage. The differences in baseline data among HLS groups were tested by ANOVA or the χ^2 test as appropriate.
†Smoking included both active (cigarettes consumption ≥ 100 in the past year) and passive (cigarettes exposure ≥ 1/d in the past year).
‡Physical activity included middle and vigorous activities during occupation, leisure time and household chores.
§Refers to non-refined cereals, such as graham bread, oats, cereal flakes, etc., calculated as dry weight.
‖Values were calculated and expressed as proteins.
¶Subjects who had insomnia for more than 6 months.
**Subjects whose Self-Rating Anxiety Scale ≥ 50.

However, the HLI may be inappropriate for assessing the risk of NAFLD since it included alcohol intake in the diet component and did not include several other NAFLD-related factors (such as BMI[8], sleep[9] and anxiety[10]). Therefore, we calculated a more comprehensive HLS by including six items (non-smoking, normal BMI, physical activity, healthy diet pattern, good sleep and no anxiety). Our results showed that the inverse association of this six-item HLS with NAFLD was robust and stable even after excluding each component in turn or replacing BMI with WC (which was a component of HLI), suggesting that it may be appropriate for the risk assessment of NAFLD (online Supplementary Table 2).

Given that each lifestyle factor may have a different association with NAFLD, simply giving equal weight to the six items of HLS may lead to misclassification. To address this issue, a weighted HLS was constructed by weighting each component based on its sβ in this study. The results showed that BMI and physical activity had the highest weights, and the OR of NAFLD in the higher weighted HLS group were lower than the OR in the higher HLS group (online Supplementary Table 2). These results suggested that the different impacts of each lifestyle factor on NAFLD should also be taken into consideration when calculating the HLS.

Table 3 Multiple logistic regression estimated OR (95 % CI) for non-alcoholic fatty liver disease (NAFLD) by Healthy Lifestyle Score (HLS) in all subjects, men and women

		Model 1*			Model 2†		
Exposures	*n* (total/cases)	OR	95 % CI	*P*-value	OR	95 % CI	*P*-value
All subjects	2981/1515						
HLS 0–1	238/142	Ref.			Ref.		
HLS 2	718/409	0·86	0·64, 1·16	0·327	0·85	0·63, 1·15	0·281
HLS 3	984/505	0·68	0·51, 0·91	0·010	0·68	0·51, 0·91	0·010
HLS 4	753/355	0·58	0·43, 0·79	<0·001	0·58	0·43, 0·78	<0·001
HLS 5–6	288/104	0·37	0·26, 0·52	<0·001	0·35	0·25, 0·51	<0·001
Men	954/515						
HLS 0–1	36/18	Ref.			Ref.		
HLS 2	235/140	1·45	0·72, 2·94	0·300	1·33	0·65, 2·75	0·440
HLS 3	342/190	1·24	0·62, 2·47	0·543	1·21	0·59, 2·45	0·604
HLS 4	235/122	1·07	0·53, 2·17	0·847	1·03	0·50, 2·13	0·936
HLS 5–6	105/45	0·76	0·35, 1·62	0·472	0·69	0·32, 1·52	0·362
Women	2027/1000						
HLS 0–1	202/124	Ref.			Ref.		
HLS 2	483/269	0·78	0·56, 1·10	0·155	0·74	0·48, 1·15	0·180
HLS 3	642/315	0·60	0·44, 0·83	0·002	0·51	0·34, 0·77	0·001
HLS 4	518/233	0·52	0·37, 0·72	<0·001	0·44	0·28, 0·67	<0·001
HLS 5–6	182/59	0·32	0·21, 0·48	<0·001	0·25	0·15, 0·41	<0·001

Ref., Reference category.
*Model 1: adjusted for age and sex (for all subjects only).
†Model 2: further adjusted for marital status, education level, household income, history of using statins and daily energy intake. For women, menopausal age and oral oestrogen use were further adjusted.

Healthy Lifestyle Score components and non-alcoholic fatty liver disease

BMI and physical activity played key roles in the inverse association of the HLS with NAFLD among the six HLS components, which was consistent with previous studies. A cross-sectional study involving 218 men aged 33–73 years indicated that the prevalence of NAFLD significantly increased with increasing BMI categories (kg/m^2) (18·5 ≤ BMI < 25·0: 1·7 %, 25·0 ≤ BMI < 30·0: 9·2 % and 30·0 ≤ BMI: 20·5 %, $P = 0·002$)[30]. A study of 18 507 Chinese individuals aged 71·4 ± 14·2 years showed that people with NAFLD had a higher BMI (kg/m^2) than those without NAFLD (25·65 *v.* 24·33, $P < 0·05$)[31]. Another retrospective study (including 1994 Chinese individuals aged 18–87 years) also showed similar results regarding the association between BMI (kg/m^2) and NAFLD (26·31 in NAFLD group *v.* 22·54 in no-NAFLD group, $P < 0·05$)[8]. People with high BMI normally have high fat consumption, which increases the synthesis of liver TAG and decreases the synthesis of very LDL. These lipid metabolic disorders can lead to an increase in fatty tissue and free fatty acids, which in turn can damage liver cells and ultimately lead to NAFLD. In addition, hyperinsulinaemia and insulin resistance are common in obese patients, and an increase in insulin can promote the synthesis of TAG, leading to the occurrence of NAFLD[32].

A cross-sectional study (*n* 349) showed that people with NAFLD participated in less resistance physical activity than people without NAFLD (13 % *v.* 23 %, $P = 0·03$), and the prevalence of NAFLD was higher for those engaging in resistance physical activity less than once a week than for those engaging at least once a week (33·9 % *v.* 18·8 %, $P < 0·01$)[33]. Another study also suggested an inverse association between fitness categories (metabolic equivalent) and the prevalence of NAFLD (metabolic equivalent < 10·2: 20·8 %, 10·2 ≤ metabolic equivalent < 11·8: 9·6 % and 11·8 ≤ metabolic equivalent: 2·7 %, $P = 0·002$)[30]. The mechanism of the beneficial effect of exercise can be concluded as a reduction in weight, liver enzymes, hepatic TAG, visceral adipose tissue volume and plasma free fatty acids[34–36] or an increase in insulin sensitivity and glucose homoeostasis[37].

Interestingly, we did not find associations of non-smoking, healthy diet pattern, good sleep and no anxiety with NAFLD in this study, although previous studies have shown inverse relationships of these four lifestyle factors with NAFLD[4,6,7,9,10] (Table 4). However, in sensitivity analyses, we found a significant synergistic association of HLS consisting of the four lifestyle factors with the presence of NAFLD (online Supplementary Table 2). This finding may be due to the synergistic effect of different components of the HLS, which enables the synergistic association of these factors to be greater than that of each part. Our findings emphasised the importance of a combined health lifestyle pattern for liver protection instead of just a single lifestyle choice.

Strengths and limitations

Several strengths of this study can be concluded. First, the sensitivity analyses showed a robust and stable inverse association between HLS and NAFLD, suggesting good internal consistency for the HLS evaluated. Second, the sample size of our study (*n* 2981) was relatively larger than that of a previous similar study (*n* 354)[20].

Table 4 Multiple logistic regression estimated OR (95 % CI) for non-alcoholic fatty liver disease (NAFLD) by individual lifestyle factors in all subjects, men and women*

	All subjects (*n*† = 2981/1515)				Men (*n* 954/515)				Women (*n* 2027/1000)			
	n	OR	95 % CI	*P*-value	*n*	OR	95 % CI	*P*-value	*n*	OR	95 % CI	*P*-value
No smoking												
No	951/499	Ref.			432/243	Ref.			519/256	Ref.		
Yes	2030/1016	0·94	0·80, 1·11	0·464	522/272	0·94	0·72, 1·24	0·676	1508/744	0·93	0·73, 1·19	0·575
Standard BMI (18·5 ≤ BMI < 24·0 kg/m^2)												
No	1084/708	Ref.			87/63	Ref.			997/645	Ref.		
Yes	1897/807	0·30	0·25, 0·36	<0·001	867/452	0·37	0·22, 0·61	<0·001	1030/355	0·28	0·23, 0·35	<0·001
Physically active (moderate or vigorous physical activity ≥ 150 min/week)												
No	1581/846	Ref.			532/309	Ref.			1049/537	Ref.		
Yes	1400/69	0·81	0·69, 0·94	0·006	422/206	0·64	0·49, 0·84	<0·001	978/463	0·87	0·71, 1·08	0·211
Healthy diet pattern (modified aMed score: 5–8)												
No	1760/895	Ref.			619/333	Ref.			1141/552	Ref.		
Yes	1221/620	0·88	0·74, 1·03	0·105	335/182	0·91	0·68, 1·21	0·505	886/448	0·87	0·70, 1·09	0·226
Good sleep (no insomnia or <6 months)												
No	178/91	Ref.			42/23	Ref.			136/69	Ref.		
Yes	2803/1424	0·73	0·53, 1·00	0·054	912/492	0·75	0·39, 1·45	0·391	1891/931	0·92	0·54, 1·56	0·743
No anxiety (Self-Rating Anxiety Scale <50)												
No	303/160	Ref.			60/27	Ref.			243/133	Ref.		
Yes	2678/1355	0·92	0·72, 1·19	0·543	594/488	1·65	0·94, 2·88	0·080	1784/867	0·75	0·53, 1·06	0·103

Modified aMed score, modified alternate Mediterranean diet score; Ref., Reference category.

*All analyses were adjusted for age, sex (for all subjects only), marital status, education level, household income, history of using statins, daily energy intake and other factors of Healthy Lifestyle Score. For women, menopausal age and oral oestrogen use were further adjusted.

†The number of total subjects and NAFLD cases, expressed as total/cases.

There are also some limitations that need to be noted. First, the data of five out of six HLS components (smoking, physical activity, diet, sleep and anxiety) were obtained by the questionnaire, and recall bias could not be completely excluded in our study. However, we conducted a face-to-face interview with the help of pictures of foods instead of self-reported questionnaires to reduce the bias. Second, the cross-sectional study design limits the possibility of inferring causality between HLS and NAFLD. However, typically, the associations will tend to be attenuated but not overestimated since healthier lifestyles would be recommended to the participants with NAFLD. Third, the validity of the physical activity questionnaire could not be obtained in this study, although the questionnaire had good long-term reliability (r 0·646, $P < 0·001$) between surveys conducted during 2008–2010 and 3 years later for the first batch subjects. Fourth, the sleep data were assessed by simply asking whether subjects had insomnia instead of using systematic questionnaires such as the Pittsburgh Sleep Quality Index. Finally, the diagnostic method of NAFLD was ultrasonography in this study, which is not the gold standard (liver biopsy). However, the reliability ($\kappa = 0·875$) and validity ($\kappa = 0·691$) of ultrasonography in this study were high, and its sensitivity (84 %) and specificity (95 %) were acceptable according to a study in the USA[38].

In conclusion, there was an inverse association between the six-item HLS and NAFLD in this middle-aged and older Chinese population, and BMI and physical activity played key roles in the association. The inverse association was more significant after weighting the HLS. Our findings suggested that a healthy lifestyle pattern (non-smoking, normal BMI, physically active, healthy diet pattern, good sleep and no anxiety) might decrease the risk of NAFLD in this population. HLS-based prospective and interventional studies are needed to address the causality problem.

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Supplementary material

For supplementary material accompanying this paper visit https://doi.org/10.1017/S1368980021000902

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