

Healthy Lifestyle Is Associated with Reduced Mortality in Patients with Non-Alcoholic Fatty Liver Disease

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Table S1. Association between healthy lifestyle categories or NAFLD status and all-cause mortality.

	Age, sex, ethnicity-adjusted		Multivariate model	
	HR(95% CI) ^a	P value	HR(95% CI) ^b	P value
Healthy Lifestyle Category				
Unfavorable Lifestyle	1 [Reference]		1 [Reference]	
Intermediate Lifestyle	0.67 (0.58-0.76)	<0.001	0.70 (0.62-0.80)	<0.001
Favorable Lifestyle	0.54 (0.45-0.63)	<0.001	0.60 (0.51-0.71)	<0.001
NAFLD				
No NAFLD	1 [Reference]		1 [Reference]	
NAFLD	1.17 (1.08-1.26)	<0.001	1.07 (0.98-1.16)	0.115
Hepatic Steatosis				
Normal	1 [Reference]		1 [Reference]	
Mild	1.16 (1.01-1.33)	0.042	1.09 (0.95-1.25)	0.196
Moderate	1.17 (1.06-1.29)	0.001	1.03 (0.93-1.13)	0.581
Severe	1.18 (0.98-1.42)	0.074	1.12 (0.94-1.33)	0.217

^a Analyses were adjusted for age, sex, ethnicity.

^b Analyses were adjusted for age, sex, ethnicity, poverty status, education level, body mass index, and prevalent comorbidities (including history of CVD, cancer, chronic bronchitis or emphysema).

Table S2. Age, sex, ethnicity-adjusted and multivariate hazard ratio of risk factor for the all-cause mortality according to healthy lifestyle factors and individual components.

	Age, sex, ethnicity-adjusted		Multivariate model	
	HR(95% CI) ^a	P value	HR(95% CI) ^b	P value
Healthy Lifestyle Score				
Score 0	1 [Reference]		1 [Reference]	
Score 1	0.74 (0.65-0.84)	<0.001	0.78 (0.68-0.89)	<0.001
Score 2	0.55 (0.47-0.65)	<0.001	0.60 (0.51-0.71)	<0.001
Score 3	0.45 (0.38-0.54)	<0.001	0.53 (0.44-0.64)	<0.001
Score 4	0.40 (0.30-0.53)	<0.001	0.49 (0.37-0.66)	<0.001
One-point increase in the healthy lifestyle score	0.77 (0.73-0.81)	<0.001	0.80 (0.76-0.85)	<0.001
Individual component of healthy lifestyle categories				
Ever smoked 100 cigarettes				
Yes	1 [Reference]		1 [Reference]	
No	0.57 (0.51-0.63)	<0.001	0.60 (0.54-0.66)	<0.001
Ever had 12 drinks				
Yes	1 [Reference]		1 [Reference]	
No	0.92 (0.77-1.11)	0.939	0.85 (0.72-1.01)	0.060
Regular physical activity				
No	1 [Reference]		1 [Reference]	
Yes	0.81 (0.72-0.90)	<0.001	0.90 (0.81-0.99)	0.039
Healthy dietary pattern				
No	1 [Reference]		1 [Reference]	
Yes	0.74 (0.67-0.83)	<0.001	0.82 (0.72-0.92)	0.001

^a Analyses were adjusted for age, sex, ethnicity.

^b Analyses were adjusted for age, sex, ethnicity, poverty status, education level, body mass index, and prevalent comorbidities (including history of hypertension, diabetes, CVD, cancer, chronic bronchitis, or emphysema).

Table S3. Association between the healthy lifestyle factors or individual components and all-cause mortality according to NAFLD status.

	NAFLD		No NAFLD	
	HR(95% CI) ^a	P value	HR(95% CI) ^a	P value
Healthy Lifestyle Category				
Score 0	1 [Reference]		1 [Reference]	
Score 1	0.78 (0.62-0.98)	0.036	0.79 (0.66-0.94)	0.009
Score 2	0.63 (0.48-0.82)	0.001	0.59 (0.47-0.74)	<0.001
Score 3	0.52 (0.39-0.70)	<0.001	0.53 (0.41-0.69)	<0.001
Score 4	0.62 (0.38-1.01)	0.057	0.39 (0.25-0.61)	<0.001
One-point increase in the healthy lifestyle score	0.82 (0.76-0.89)	<0.001	0.79 (0.73-0.86)	<0.001
Individual component of healthy lifestyle categories				
Ever smoked 100 cigarettes				
Yes	1 [Reference]		1 [Reference]	
No	0.59 (0.50-0.70)	<0.001	0.60 (0.52-0.69)	<0.001
Ever had 12 drinks				
Yes	1 [Reference]		1 [Reference]	
No	0.88 (0.69-1.13)	0.309	0.79 (0.66-0.96)	0.016
Regular physical activity				
No	1 [Reference]		1 [Reference]	
Yes	0.89 (0.72-1.10)	0.281	0.93 (0.83-1.05)	0.250
Healthy dietary pattern				
No	1 [Reference]		1 [Reference]	
Yes	0.91 (0.77-1.09)	0.300	0.75 (0.65-0.88)	<0.001

^a Analyses were adjusted for age, sex, ethnicity, poverty status, education level, body mass index, and prevalent comorbidities (including history of hypertension, diabetes, CVD, cancer, chronic bronchitis, or emphysema).

Table S4. Risk of mortality according to lifestyle categories after excluding incidents during the first year of follow-up

No. of total	1990 (56.56%)	1049 (28.62%)	537 (14.81%)	3303 (53.86%)	1894 (29.24%)	990 (16.89%)
No. of cases/ Person years	176/39496	80/21491	31/11289	264/69278	89/41278	54/21326
HR (95% CI) ^a	1 [Reference]	0.83 (0.55-1.27)	0.49 (0.27-0.90)	1 [Reference]	0.40 (0.29-0.57)	0.41 (0.25-0.68)
P value ^a		0.396	0.022		<0.001	<0.001
P value for trend ^a		0.007			<0.001	
Absolute risk, % (95% CI)	8.84 (7.65-10.20)	7.63 (6.13-9.44)	5.77 (4.02-8.18)	7.99 (7.10-8.98)	4.70 (3.81-5.78)	5.45 (4.16-7.11)
Incidence rate per 1000 PYs (95% CI) ^b	3.33 (2.79-3.97)	2.67 (2.09-3.41)	1.96 (1.35-2.85)	2.66 (2.29-3.09)	1.37 (1.08-1.73)	1.42 (1.06-1.91)
Numbers needed -20 years ^c		136	45		35	36

^a Adjusted for age, sex, ethnicity, poverty status, education level, body mass index, and prevalent comorbidities (including history of hypertension, diabetes, CVD, cancer, chronic bronchitis, or emphysema).

^b Incidence rate for liver cancer are adjusted for age at baseline, gender, and ethnicity.

^c The numbers needed to adhere to a healthy lifestyle to prevent one death in 20 years.

Table S5. Risk of mortality according to lifestyle categories after excluding incidents during the first three years of follow-up.

No. of total	1985 (56.66%)	1044 (28.51%)	534 (14.83%)	3293 (53.85%)	1889 (29.22%)	987 (16.93%)
No. of cases/ Person years	171/39484	75/21482	28/11284	254/69261	84/41266	51/21320
HR (95% CI) ^a	1 [Reference]	0.76 (0.49-1.18)	0.47 (0.25-0.87)	1 [Reference]	0.39 (0.28-0.55)	0.42 (0.25-0.70)
P value ^a		0.221	0.017		<0.001	0.001
P value for trend ^a		0.003			<0.001	
Absolute risk, % (95% CI)	8.61 (7.44-9.96)	7.18 (5.73-8.96)	5.24 (3.58-7.58)	7.71 (6.384-8.69)	4.45 (3.58-5.50)	5.17 (3.91-6.79)
Incidence rate per 1000 PYs (95% CI) ^b	3.26 (2.72-3.90)	2.51 (1.95-3.23)	1.76 (1.19-2.61)	2.60 (2.23-3.03)	1.32 (1.04-1.67)	1.37 (1.01-1.85)
Numbers needed -20 years ^c	98	44			35	37

^a Adjusted for age, sex, ethnicity, poverty status, education level, body mass index, and prevalent comorbidities (including history of hypertension, diabetes, CVD, cancer, chronic bronchitis, or emphysema).

^b Incidence rate for liver cancer are adjusted for age at baseline, gender, and ethnicity.

^c The numbers needed to adhere to a healthy lifestyle to prevent one death in 20 years.

Table S6. Multivariable-adjusted HRs (95% CIs) for mortality by healthy lifestyle categories according to baseline characteristics.

Subgroups		No. of total	No. of All-caus e mortality	No. of Cardiovas cular mortality	No. of Cancer mortali ty	Person years	All-cause mortality		Cardiovascular mortality		Cancer mortality	
							HR(95%CI) ^a	P value ^a	HR(95%CI) ^a	P value ^a	HR(95%CI) ^a	P value ^a
Age at baseline, years												
<50	Unfavorable	1,120	175	40	46	25,267	1 [Reference]		1 [Reference]		1 [Reference]	
	Intermediate	583	69	16	19	13,249	0.96 (0.59-1.56)	0.862	1.72 (0.55-5.36)	0.346	0.81 (0.35-1.86)	0.621
	Favorable	297	20	7	3	6,787	0.42 (0.18-1.01)	0.051	0.40 (0.14-1.14)	0.085	0.46 (0.11-2.01)	0.302
	Unfavorable	872	606	185	132	14,231	1 [Reference]		1 [Reference]		1 [Reference]	
	Intermediate	466	284	79	61	8,242	0.84 (0.69-1.02)	0.078	0.69 (0.48-1.01)	0.055	1.00 (0.65-1.54)	0.994
	Favorable	240	129	37	28	4,503	0.84 (0.64-1.11)	0.222	0.81 (0.49-1.32)	0.392	0.64 (0.36-1.15)	0.136
Gender												
Male	Unfavorable	1,119	505	160	108	21,399	1 [Reference]		1 [Reference]		1 [Reference]	
	Intermediate	411	143	36	33	8,389	0.69 (0.52-0.92)	0.011	0.41 (0.26-0.64)	<0.00 1	0.86 (0.47-1.58)	0.622
	Favorable	122	33	9	10	2,513	0.66	0.094	0.72	0.433	0.71	0.384

								(0.40-1.07)		(0.32-1.63)		(0.32-1.54)	
								1 [Reference]		1 [Reference]		1 [Reference]	
		Unfavorable	873	276	65	70	18,098	0.80 (0.63-1.01)	0.062	1.01 (0.59-1.75)	0.963	0.76 (0.47-1.21)	0.247
Female	Intermediate	638	210	59	47	13,103	0.66 (0.52-0.85)	0.001	0.65 (0.39-1.08)	0.096	0.44 (0.22-0.88)	0.021	
	Favorable	415	116	35	21	8,777							
Ethnicity								1 [Reference]		1 [Reference]		1 [Reference]	
Non-Hispanic white	Unfavorable	779	341	97	82	15,178	0.74 (0.57-0.96)	0.024	0.65 (0.38-1.10)	0.107	0.85 (0.52-1.39)	0.526	
	Intermediate	384	169	50	41	7,521	0.57 (0.43-0.75)	<0.001	0.51 (0.31-0.83)	0.007	0.43 (0.22-0.83)	0.013	
	Favorable	206	77	20	16	4,209							
Non-Hispanic black	Unfavorable	487	208	54	45	9,375	0.52 (0.37-0.74)	<0.001	0.56 (0.28-1.12)	0.102	0.49 (0.24-0.99)	0.047	
	Intermediate	246	62	13	12	5,303	0.72 (0.45-1.15)	0.167	1.36 (0.60-3.06)	0.458	0.43 (0.16-1.15)	0.092	
	Favorable	124	28	12	4	2,593							
Mexican-American	Unfavorable	660	217	69	49	13,569	1 [Reference]	1 [Reference]		1 [Reference]		1 [Reference]	
	Intermediate	376	117	32	26	7,690	1.20 (0.91-1.58)	0.204	0.83 (0.43-1.60)	0.571	0.94 (0.49-1.80)	0.860	
	Favorable	174	37	10	10	3,780	0.65 (0.40-1.05)	0.079	0.62 (0.21-1.81)	0.382	0.45 (0.18-1.15)	0.096	

Others	Unfavorable	66	15	5	2	1,377	1 [Reference]	1 [Reference]		1 [Reference]	
	Intermediate	43	5	0	1	978	0.56 (0.20-1.52)	0.253	(-)	(-)	(-)
	Favorable	33	7	2	1	708	1.64 (0.39-6.95)	0.503	(-)	(-)	(-)
Poverty status											
Yes	Unfavorable	499	201	53	49	9,670	1 [Reference]	1 [Reference]		1 [Reference]	
	Intermediate	227	73	18	15	4,692	0.39 (0.26-0.57)	<0.001	0.56 (0.25-1.29)	0.173	0.28 (0.10-0.77)
	Favorable	147	36	11	7	3,075	0.51 (0.32-0.81)	0.005	0.57 (0.20-1.64)	0.300	0.18 (0.04-0.75)
No	Unfavorable	1,493	580	172	129	29,828	1 [Reference]	1 [Reference]		1 [Reference]	
	Intermediate	822	280	77	65	16,799	0.81 (0.63-1.03)	0.086	0.68 (0.42-1.08)	0.101	1.01 (0.65-1.58)
	Favorable	390	113	33	24	8,214	0.65 (0.51-0.84)	0.001	0.60 (0.37-0.96)	0.034	0.58 (0.32-1.07)
Education											
Less than high school	Unfavorable	909	457	143	98	16,916	1 [Reference]	1 [Reference]		1 [Reference]	
	Intermediate	390	178	47	39	7,480	0.73 (0.52-1.02)	0.068	0.48 (0.27-0.88)	0.017	0.94 (0.38-2.36)
	Favorable	218	82	27	17	4,367	0.78 (0.48-1.25)	0.298	0.52 (0.26-1.03)	0.060	0.81 (0.34-1.95)

High school or above	Unfavorable	1,083	324	82	80	22,582	1 [Reference]	0.76 (0.59-0.98)	0.035	0.79 (0.44-1.42)	0.428 (0.51-1.23)
	Intermediate	659	175	48	41	14,011					
	Favorable	319	67	17	14	6,923	0.58 (0.41-0.83)			0.64 (0.38-1.10)	0.105 (0.20-0.76)
Body mass index (kg/m²)											
<25	Unfavorable	462	156	39	34	9,299	1 [Reference]	0.68 (0.48-0.96)	0.030	0.70 (0.28-1.72)	0.432 (0.49-2.58)
	Intermediate	252	59	14	21	5,394					
	Favorable	163	35	8	7	3,540	0.55 (0.36-0.84)			0.69 (0.34-1.39)	0.298 (0.14-0.90)
≥25	Unfavorable	1,530	625	186	144	30,199	1 [Reference]	0.76 (0.58-0.98)	0.037	0.64 (0.41-1.00)	0.049 (0.52-1.30)
	Intermediate	797	294	81	59	16,097					
	Favorable	374	114	36	24	7,750	0.67 (0.50-0.89)			0.56 (0.31-1.00)	0.049 (0.29-1.06)
Waist circumference (cm)											
men < 90 and women < 85	Unfavorable	387	91	20	19	8,276	1 [Reference]	0.77	0.262	0.76	0.721 (1.69-0.254)
	Intermediate	232	34	6	14	5,150					

						(0.48-1.22)		(0.16-3.48)		(0.69-4.14)		
		Favorable	151	23	3	7	3,348	0.51 (0.28-0.91)	0.28 (0.04-2.10)	0.215	0.75 (0.22-2.53)	0.639
men \geq 90 and women \geq 85	Unfavorable	1,562	668	196	155	30,476	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]		
	Intermediate	792	308	86	66	15,875	0.73 (0.58-0.91)	0.005	0.66 (0.43-0.99)	0.045	0.80 (0.50-1.28)	0.353
	Favorable	372	119	38	24	7,704	0.64 (0.49-0.83)	0.001	0.60 (0.39-0.94)	0.027	0.49 (0.25-0.98)	0.043
Hypertension												
Yes	Unfavorable	826	474	151	98	14,588	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]		
	Intermediate	427	220	69	45	8,042	0.73 (0.54-1.00)	0.050	0.69 (0.44-1.10)	0.123	0.96 (0.57-1.61)	0.875
	Favorable	202	98	33	19	3,852	0.70 (0.51-0.97)	0.031	0.74 (0.47-1.15)	0.180	0.62 (0.28-1.36)	0.231
No	Unfavorable	1,166	307	74	80	24,910	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]		
	Intermediate	622	133	26	35	13,449	0.78 (0.61-0.99)	0.044	0.61 (0.25-1.50)	0.280	0.72 (0.39-1.31)	0.278
	Favorable	335	51	11	12	7,437	0.58 (0.40-0.84)	0.004	0.35 (0.13-1.00)	0.050	0.40 (0.16-1.01)	0.052
Diabetes												
Yes	Unfavorable	368	245	75	40	6,136	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]		
	Intermediate	180	119	33	22	2,889	0.73	0.126	0.65	0.229	1.14	0.787

						(0.49-1.09)		(0.32-1.31)		(0.43-3.04)		
		Favorable	81	41	11	2	1,494	0.79 (0.45-1.39)	0.417	0.86 (0.28-2.64)	0.798	0.02 (0.00-0.12) <0.001
		Unfavorable	1,624	536	150	138	33,361	1 [Reference]		1 [Reference]	1 [Reference]	
No		Intermediate	869	234	62	58	18,603	0.76 (0.60-0.96)	0.022	0.69 (0.40-1.20)	0.190	0.77 (0.49-1.21) 0.262
		Favorable	456	108	33	29	9,796	0.61 (0.45-0.83)	0.001	0.55 (0.33-0.92)	0.023	0.55 (0.28-1.06) 0.074
CVD												
		Unfavorable	191	146	62	27	2,590	1 [Reference]		1 [Reference]	1 [Reference]	
Yes		Intermediate	79	67	23	10	1,023	0.74 (0.52-1.06)	0.098	0.52 (0.29-0.92)	0.025	1.23 (0.41-3.64) 0.711
		Favorable	20	15	6	1	316	0.74 (0.29-1.88)	0.524	0.84 (0.19-3.65)	0.816	0.29 (0.03-2.64) 0.273
		Unfavorable	1,801	635	163	151	36,908	1 [Reference]		1 [Reference]	1 [Reference]	
No		Intermediate	970	286	72	70	20,468	0.74 (0.57-0.96)	0.026	0.71 (0.37-1.35)	0.297	0.81 (0.50-1.33) 0.413
		Favorable	517	134	38	30	10,973	0.63 (0.49-0.80)	<0.001	0.56 (0.33-0.94)	0.030	0.50 (0.26-0.98) 0.044
Cancer												
		Unfavorable	120	78	18	25	1,981	1 [Reference]		1 [Reference]	1 [Reference]	
Yes		Intermediate	50	28	6	9	884	0.68	0.182	0.48	0.199	0.55 0.288

								(0.39-1.20)	(0.15-1.48)	(0.18-1.67)			
		Favorable	27	16	7	4	439	0.74 (0.43-1.28)	0.282	1.92 (0.75-4.92)	0.173	0.38 (0.15-1.02)	0.054
		Unfavorable	1,872	703	207	153	37,517	1 [Reference]		1 [Reference]		1 [Reference]	
No	Intermediate		999	325	89	71	20,607	0.76 (0.61-0.94)	0.010	0.67 (0.42-1.07)	0.095	0.92 (0.61-1.39)	0.692
	Favorable		510	133	37	27	10,851	0.63 (0.48-0.84)	0.002	0.47 (0.30-0.75)	0.002	0.51 (0.25-1.07)	0.075
Emphysema or chronic bronchitis													
		Unfavorable	168	96	24	25	2,843	1 [Reference]		1 [Reference]		1 [Reference]	
Yes	Intermediate		55	26	8	4	958	0.73 (0.36-1.47)	0.377	0.39 (0.15-0.98)	0.045	(-)	(-)
	Favorable		25	8	3	0	517	0.45 (0.30-0.67)	<0.001	0.63 (0.15-2.62)	0.526	(-)	(-)
		Unfavorable	1,824	685	201	153	36,655	1 [Reference]		1 [Reference]		1 [Reference]	
No	Intermediate		994	327	87	76	20,533	0.73 (0.59-0.89)	0.003	0.62 (0.37-1.04)	0.071	0.90 (0.57-1.41)	0.643
	Favorable		512	141	41	31	10,773	0.65 (0.51-0.84)	0.001	0.57 (0.35-0.92)	0.020	0.57 (0.31-1.03)	0.064

^a Adjusted for age, sex, ethnicity, poverty status, education level, body mass index, and prevalent comorbidities (including history of hypertension, diabetes, CVD, cancer, chronic bronchitis, or emphysema).

Table S7. Association between combinations of the healthy lifestyle factors (Prevalence >5%) and risk of liver cancer.

Healthy lifestyle score	SMK	ALCO	DIET	PA	Prevalence (%)	All-cause mortality		Cardiovascular mortality		Cancer mortality	
						Hazard Ratio (95% CI) ^a	P value ^a	Hazard Ratio (95% CI) ^a	P value ^a	Hazard Ratio (95% CI) ^a	P value ^a
NAFLD											
Score 0					753 (22.06)	1 [Reference]		1 [Reference]		1 [Reference]	
					247 (8.48)	0.82 (0.56-1.20)	0.303	0.67 (0.34-1.34)	0.258	0.99 (0.53-1.85)	0.967
Score 1					447 (12.52)	0.87 (0.67-1.14)	0.325	0.90 (0.54-1.48)	0.678	0.61 (0.37-1.00)	0.051
					491 (12.28)	0.53 (0.36-0.77)	0.001	0.58 (0.25-1.34)	0.202	0.47 (0.22-1.01)	0.052
Score 2					226 (8.21)	0.76 (0.54-1.07)	0.116	0.73 (0.30-1.80)	0.498	0.93 (0.46-1.87)	0.837
					191 (5.83)	0.43 (0.30-0.61)	<0.001	0.57 (0.35-0.95)	0.029	0.33 (0.12-0.91)	0.033
Score 3					371 (9.12)	0.52 (0.36-0.75)	<0.001	0.30 (0.17-0.55)	<0.001	0.41 (0.19-0.87)	0.021
					211 (7.47)	0.54 (0.37-0.80)	0.002	0.40 (0.18-0.90)	0.027	0.31 (0.12-0.75)	0.010
No NAFLD											
Score 0					1261 (21.28)	1 [Reference]		1 [Reference]		1 [Reference]	
					587 (11.06)	1.02 (0.83-1.25)	0.857	1.39 (0.87-2.21)	0.169	0.85 (0.51-1.41)	0.526
Score 1					570 (9.46)	0.81 (0.64-1.04)	0.100	0.93 (0.62-1.40)	0.738	0.54 (0.29-1.00)	0.051
					795 (11.05)	0.44 (0.31-0.62)	<0.001	0.67 (0.36-1.26)	0.214	0.30 (0.14-0.66)	0.003
Score 2					409 (8.35)	0.61 (0.47-0.78)	<0.001	0.83 (0.51-1.36)	0.462	0.29 (0.16-0.50)	<0.001
					496 (8.16)	0.64 (0.45-0.91)	0.013	0.59 (0.27-1.29)	0.188	0.37 (0.17-0.80)	0.011
Score 3					588 (8.62)	0.51 (0.38-0.69)	<0.001	0.89 (0.49-1.62)	0.708	0.21 (0.10-0.42)	<0.001
					467 (9.79)	0.56 (0.43-0.74)	<0.001	0.44 (0.26-0.75)	0.003	0.40 (0.21-0.78)	0.008

^a Adjusted for age, sex, ethnicity, poverty status, education level, body mass index, and prevalent comorbidities (including history of hypertension, diabetes, CVD, cancer, chronic bronchitis, or emphysema).

Figure S1. Association between combinations of the healthy lifestyle factors (Proportion >5%) and risk of all-cause mortality/cardiovascular mortality/cancer mortality in the sub cohort without NAFLD. Adjusted for age, sex, ethnicity, poverty status, education level, body mass index, and prevalent comorbidities (including history of hypertension, diabetes, CVD, cancer, chronic bronchitis or emphysema).

