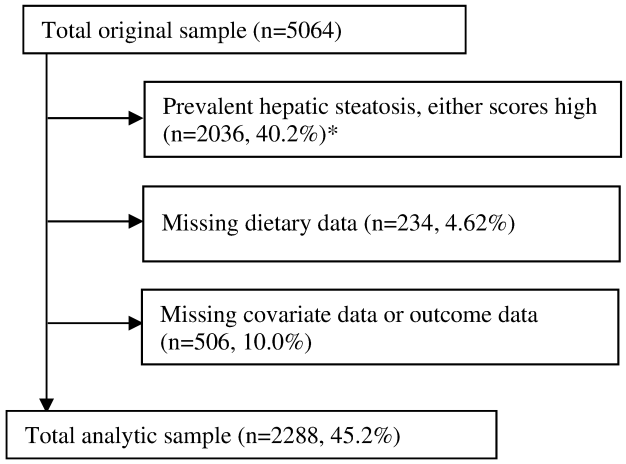
Supplementary file

Title: The association between adherence to the Mediterranean diet and hepatic steatosis: the Swiss CoLaus prospective cohort study

Table of Content

Figure S1 Sample selection flow chart.



* Prevalent hepatic steatosis was defined as having either fatty liver index≥ 60 OR non-alcoholic fatty liver disease fatty liver score≥ -0.640.

Table S1 Characteristics of the participants included and excluded from the analysis, CoLaus study, Switzerland.

Characteristic	Included (n=2288)	Excluded (n=2776)	*P*-value*
Age, *years*	55.8±10.0	59.4±10.6	<0.001
Women (%)	65.4	43.6	<0.001
Marital status (%)†			0.038
Single	16.5	14.0	
Married/cohabiting	56.6	57.4	
Widowed/separated/divorced	26.8	28.6	
Employed (%)	63.5	50.4	<0.001
Education (%)†			<0.001
University	25.9	17.5	
High school	28.5	23.6	
Apprenticeship	33.2	37.4	
Mandatory education	12.5	21.4	
Current smoker (%)	20.1	23.1	<0.001
Alcohol consumption (%)†‡			<0.001
Abstainers	23.5	26.8	
Moderate	69.3	63.3	
Heavy	7.2	9.9	
Total energy intake (kcal/d)	1807±673	1853±784	0.033
Total protein (% energy)	15.4±3.3	15.6±3.5	0.015
Total carbohydrate (% energy)	47.0±8.6	45.4±9.1	<0.001
Total fat (% energy)	34.3±6.7	34.4±6.9	0.54
TEE (kcal/d)	2575±586	2790±669	<0.001
Metabolic syndrome (%)§	10.8	60.9	<0.001
BMI (kg/m^2)	23.7±2.8	28.3±4.8	<0.001
Waist circumference (cm)	84.4±8.9	98.3±12.5	<0.001
Triglycerides (mmol/l)	1.0±0.5	1.6±1.1	<0.001
median (iqr)	0.9 (0.7, 1.2)	1.4 (1.0, 2.0)	
GGT (U/l)	23.8±16.0	48.8±60.8	<0.001
median (iqr)	19 (14, 27)	32 (21, 53)	
≥50 (%)	5.6	27.5	<0.001
ALT (U/l)	21.8±8.8	32.5±20.7	<0.001
median (iqr)	20 (16, 25)	27 (20, 38)	
≥40 (%)	5.0	23.3	<0.001
AST (U/l)	25.9±6.2	31.6±14.1	<0.001
median (iqr)	25 (22, 29)	28 (24, 34)	
≥37 (%)	5.6	20.4	<0.001

Abbreviations: TEE, total energy expenditure; BMI, body mass index; iqr, interquartile range; GGT, gamma-glutamyl transferase; ALT, alanine aminotransferase; AST, aspartate aminotransferase.
Data are mean ± SD for continuous variables or percent for categorical variables, unless otherwise stated.
* P-value calculated using Chi-square test for categorical variables and student's t-test for continuous variables.
† Due to some missing data, percentages do not always add to 100%.
‡ Alcohol consumption categorized as "abstainers" (0 unit/week), "moderate" (1–21 units/week for men, 1–14 for women), and "heavy drinkers" (>21 units/week for men, >14 for women).
§ Metabolic syndrome defined according to the International Diabetic Federation (waist circumference ≥94 cm in men and ≥80 cm in women plus at least two of the following factors: serum triglycerides≥1.70 mmol/L or specific treatment for this lipid abnormality; serum high-density lipoprotein cholesterol <1.03 mmol/L in men and <1.29 mmol/L in women or specific treatment for this lipid abnormality; systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg or treatment for previously diagnosed hypertension; and fasting plasma glucose ≥5.6 mmol/L or previously diagnosed type 2 diabetes).

Table S2 Baseline characteristics of the participants according to the risk of hepatic steatosis defined by the fatty liver index or the NAFLD-score, CoLaus study, Switzerland.

	Risk of hepatic steatosis					
	FLI			NAFLD-score		
Characteristic	No (n=2135)	Yes (n=153)	*P*-value*	No (n=2080)	Yes (n=208)	*P*-value*
Age, *years*	55.8±10.1	54.9±9.5	0.29	55.6±10	57.7±10.1	0.003
Women (%)	66.8	45.8	<0.001	66.7	52.9	<0.001
Marital status (%)†			0.86			0.79
Single	16.6	15.0		16.7	14.9	
Married/cohabiting	56.5	58.2		56.5	58.2	
Widowed/Separated/divorced	26.8	26.8		26.8	26.9	
Employed (%)	63.3	66.0	0.50	64.5	53.8	0.002
Education (%)†			0.013			0.33
University	26.7	15.0		26.4	20.7	
High school	28.3	30.1		28.3	29.8	
Apprenticeship	32.6	40.5		32.8	36.5	
Mandatory education	12.3	14.4		12.4	13.0	
Current smoker (%)	19.7	25.5	0.006	20.3	17.8	0.52
Alcohol consumption (%)†‡			0.15			0.001
Abstainers	23.3	26.1		22.5	33.7	
Moderate	69.7	63.4		70.4	58.7	
Heavy	6.9	10.5		7.1	7.7	
Total energy intake (kcal/d)	1800±655	1906±879	0.062	1794±654	1938±833	0.003
Protein (% energy)	15.3±3.1	16.1±5.0	0.006	15.3±3.2	16.0±4.1	0.006
Carbohydrate (% energy)	47.1±8.5	45.6±10.1	0.037	47.0±8.5	46.5±9.5	0.36
Fat (% energy)	34.3±6.7	33.8±7.2	0.37	34.2±6.7	34.4±6.6	0.69
TEE (kcal/d)	2552±572	2912±677	<0.001	2562±582	2699±616	0.002
Metabolic syndrome (%)§	9.9	22.9	<0.001	9.8	21.2	<0.001
BMI (kg/m^2)	23.5±2.7	26.8±2.6	<0.001	23.5±2.8	26.0±2.5	<0.001
Waist circumference (cm)	83.8±8.7	93.4±7.0	<0.001	83.7±8.7	92.0±7.4	<0.001
Triglycerides (mmol/l)	1.0±0.5	1.2±0.5	<0.001	1.0±0.5	1.2±0.5	<0.001
median (iqr)	0.9 (0.7, 1.2)	1.1 (0.7, 1.2)		0.9 (0.7, 1.2)	1.1 (0.8, 1.4)	
GGT (U/l)	23.1±15.2	32.4±22.2	<0.001	23.3±15.4	28.1±20.6	<0.001
median (iqr)	19 (14, 26)	26 (18, 40)		19 (14, 26)	22 (15, 34)	
≥50 (%)	4.9	15.0	<0.001	5.3	9.1	0.022
ALT (U/l)	21.6±8.8	23.5±8.9	0.013	21.3±8.4	26.0±11.6	<0.001
median (iqr)	19 (16, 25)	21 (17, 28)		19 (16, 25)	23 (18, 30)	
≥40 (%)	5.0	5.9	0.63	4.5	10.6	<0.001
AST (U/l)	25.9±6.2	26.3±6.3	0.50	25.9±6.2	26.9±6.2	0.026
median (iqr)	25 (22, 29)	25 (22, 29)		25 (22, 29)	26 (22, 30)	
≥37 (%)	5.5	7.2	0.39	5.3	8.2	0.096

Abbreviations: TEE, total energy expenditure; FLI, fatty liver index; NAFLD, non-alcoholic fatty liver disease; BMI, body mass index; iqr, interquartile range; GGT, gamma-glutamyl transferase; ALT, alanine aminotransferase; AST, aspartate Aminotransferase.

Data are mean ± SD for continuous variables or percent for categorical variables, unless otherwise stated.

* P-value calculated using Chi-square test for categorical variables and student's t-test for continuous variables.

† Due to some missing data, percentages do not always add to 100%.

‡ Alcohol consumption categorized as "abstainers" (0 unit/week), "moderate" (1–21 units/week for men, 1–14 for women), and "heavy drinkers" (>21 units/week for men, >14 for women).

§ Metabolic syndrome defined according to the International Diabetic Federation (waist circumference ≥94 cm in men and ≥80 cm in women plus at least two of the following factors: serum triglycerides≥1.70 mmol/L or specific treatment for this lipid abnormality; serum high-density lipoprotein cholesterol <1.03 mmol/L in men and <1.29 mmol/L in women or specific treatment for this lipid abnormality; systolic blood pressure ≥130 mm Hg or diastolic blood pressure ≥85 mm Hg or treatment for previously diagnosed hypertension; and fasting plasma glucose ≥5.6 mmol/L or previously diagnosed type 2 diabetes.

Table S3 Prospective association of the Mediterranean diet score with the risk of hepatic steatosis, CoLaus study, Switzerland: assessment of influence of other potential covariates.

	Risk ratio (95% CI) across quintiles of Mediterranean diet score*					*P*-trend	Risk ratio (95% CI) Per SD increase*
	Q1	Q2	Q3	Q4	Q5		
Range	1.83-7.63	7.64-8.35	8.36-8.92	8.93-9.59	9.60-12.1		
N total	458	458	457	458	457		
Fatty liver index†							
Different models							
N Cases (score≥60)	36	43	35	22	17		
Multivariable (Model 1)‡	1.00 (ref.)	1.11 (0.72, 1.72)	1.07 (0.68, 1.66)	0.71 (0.42, 1.22)	0.50 (0.28, 0.91)	0.006	0.84 (0.71, 0.99)
Model 1 + Changes in BMI categories§	1.00 (ref.)	1.11 (0.73, 1.69)	0.98 (0.64, 1.50)	0.73 (0.43, 1.24)	0.59 (0.32, 1.06)	0.024	0.85 (0.72, 1.02)
Model 1 + Alcohol	1.00 (ref.)	1.11 (0.72, 1.72)	1.06 (0.69, 1.65)	0.71 (0.41, 1.22)	0.50 (0.28, 0.91)	0.006	0.84 (0.70, 0.99)
Model 1 + Alcohol+ BMI‖	1.00 (ref.)	1.13 (0.74, 1.73)	0.92 (0.59, 1.42)	0.76 (0.45, 1.29)	0.63 (0.35, 1.14)	0.047	0.86 (0.72, 1.04)
Model 1 + Clinical variables**	1.00 (ref.)	1.30 (0.80, 2.11)	1.20 (0.74, 1.94)	0.77 (0.43, 1.39)	0.57 (0.30, 1.09)	0.023	0.84 (0.70, 1.01)
Model 1 + Clinical variables + BMI	1.00 (ref.)	1.28 (0.79, 2.07)	0.94 (0.58, 1.52)	0.80 (0.45, 1.41)	0.68 (0.36, 1.27)	0.076	0.86 (0.71, 1.04)
Model 1 + MetS††	1.00 (ref.)	1.14 (0.74, 1.75)	1.03 (0.66, 1.60)	0.68 (0.40, 1.16)	0.51 (0.28, 0.93)	0.005	0.83 (0.70, 0.99)
NAFLD-score‡‡							
Different models							
N Cases (score≥-0.640)	41	46	51	38	32		
Multivariable (Model 1)‡	1.00 (ref.)	1.13 (0.75, 1.70)	1.26 (0.85, 1.87)	1.01 (0.65, 1.56)	0.80 (0.50, 1.28)	0.28	0.95 (0.82, 1.10)
Model 1 + Changes in BMI categories§	1.00 (ref.)	1.13 (0.76, 1.69)	1.18 (0.80, 1.74)	1.04 (0.68, 1.60)	0.93 (0.58, 1.48)	0.65	0.99 (0.86, 1.16)
Model 1 + Alcohol	1.00 (ref.)	1.11 (0.73, 1.67)	1.22 (0.82, 1.82)	0.97 (0.63, 1.51)	0.77 (0.48, 1.23)	0.21	0.94 (0.81, 1.09)
Model 1 + Alcohol+ BMI‖	1.00 (ref.)	1.16 (0.78, 1.73)	1.15 (0.78, 1.68)	1.04 (0.68, 1.61)	0.93 (0.58, 1.48)	0.62	0.99 (0.85, 1.15)
Model 1 + Clinical variables**	1.00 (ref.)	1.20 (0.78, 1.84)	1.32 (0.88, 1.98)	0.99 (0.64, 1.55)	0.85 (0.52, 1.37)	0.33	0.95 (0.82, 1.11)
Model 1 + Clinical variables + BMI	1.00 (ref.)	1.21 (0.80, 1.84)	1.19 (0.80, 1.78)	1.06 (0.69, 1.64)	0.99 (0.61, 1.60)	0.76	0.99 (0.85, 1.16)

Abbreviations: SES, socio-economic status; BMI, body mass index; MetS, metabolic syndrome; NAFLD, non-alcoholic fatty liver disease; SD, standard deviation; CI, confidence interval.

Statistical analysis using Poisson regression with robust standard errors; results are expressed as risk ratios and (95% confidence intervals).

* In categorical analysis, the population was divided into five groups by quintiles (Q1-Q5) of the Mediterranean diet score; Standard deviation was 1.20 for different multivariable analyses.

† Calculated based on an algorithm including BMI, waist circumference, triglycerides, and gamma-glutamyl transferase.

‡ Adjusted for age (years), sex, marital status (single, married/cohabitant, and widowed/Separated/divorced), occupational status (working and not working), education level (university, high school, apprenticeship, and mandatory education), smoking status (never, former, and current), energy intake (kcal/day), total energy expenditure (kcal/day), and date of dietary assessment.

§ Changes in BMI categories defined as individuals with a normal BMI at baseline and follow-up, individuals with normal BMI at baseline and overweight or obese BMI at follow-up, individuals with overweight or obese BMI at baseline and at follow-up, or individuals with overweight or obese BMI at baseline and normal at follow-up.

‖ Results of further adjustment for waist circumference were broadly in line with of the further adjustment for BMI (data not shown).

**Family history of diabetes (yes/no), high blood pressure (yes/no), high triglyceride level (yes/no), low HDL level (yes/no), and high glucose level (yes/no).

†† Metabolic syndrome as defined by the International Diabetes Federation (yes/no).

‡‡ Calculated based on an algorithm including presence of the metabolic syndrome and type 2 diabetes, and concentrations of fasting serum insulin, fasting serum aspartate-aminotransferase (AST), and the AST/alanine-aminotransferase ratio.

Table S4 Sensitivity analyses for the associations of the Mediterranean diet score with the risk of hepatic steatosis, CoLaus study, Switzerland.

	Risk ratio (95% CI) across quintiles of Mediterranean diet score*						
	Q1	Q2	Q3	Q4	Q5	*P*-trend	Risk ratio (95% CI) Per SD increase*
Range	1.83-7.63	7.64-8.35	8.36-8.92	8.93-9.59	9.60-12.1		
N total	458	458	457	458	457		
Fatty liver index†							
Different models							
N Cases (score≥60)	36	43	35	22	17		
Multivariable (Model 1)‡	1.00 (ref.)	1.11 (0.72, 1.72)	1.07 (0.68, 1.66)	0.71 (0.42, 1.22)	0.50 (0.28, 0.91)	0.006	0.84 (0.71, 0.99)
Excluding alcohol from MDS component							
Model 1 + Alcohol	1.00 (ref.)	1.64 (1.04, 2.58)	1.08 (0.65, 1.80)	1.17 (0.70, 1.96)	0.65 (0.35, 1.18)	0.069	0.86 (0.73, 1.03)
Model 1 + Alcohol + BMI§	1.00 (ref.)	1.53 (0.98, 2.39)	0.94 (0.57, 1.54)	1.08 (0.67, 1.77)	0.75 (0.41, 1.35)	0.15	0.89 (0.75, 1.06)
Excluding participants with BMI≥30‖							
N Cases (score≥60)	35	40	28	19	16		
Model 1	1.00 (ref.)	1.08 (0.69, 1.68)	0.90 (0.56, 1.46)	0.64 (0.36, 1.12)	0.50 (0.27, 0.93)	0.005	0.83 (0.69, 0.98)
Model 1 + BMI§	1.00 (ref.)	1.02 (0.66, 1.58)	0.84 (0.53, 1.33)	0.65 (0.37, 1.14)	0.60 (0.33, 1.10)	0.031	0.85 (0.70, 1.02)
Excluding participants with excessive alcohol consumption**							
N Cases (score≥60)	33	42	34	21	17		
Model 1	1.00 (ref.)	1.17 (0.75, 1.84)	1.12 (0.71, 1.77)	0.70 (0.40, 1.23)	0.52 (0.28, 0.95)	0.007	0.82 (0.69, 0.98)
Model 1 + BMI§	1.00 (ref.)	1.17 (0.76, 1.81)	0.91 (0.58, 1.42)	0.73 (0.42, 1.24)	0.64 (0.35, 1.15)	0.037	0.85 (0.71, 1.02)
Excluding participants with implausible energy intake††							
N Cases (score≥60)	33	41	33	22	16		
Model 1	1.00 (ref.)	1.19 (0.63, 2.23)	1.16 (0.61, 2.20)	0.87 (0.45, 1.69)	0.69 (0.35, 1.38)	0.16	0.85 (0.71, 1.01)
Model 1 + BMI§	1.00 (ref.)	1.13 (0.60, 2.13)	0.90 (0.47, 1.73)	0.81 (0.43, 1.53)	0.74 (0.37, 1.49)	0.20	0.86 (0.72, 1.04)
Excluding participants with secondary causes of hepatic steatosis‡‡							
N Cases (score≥60)	37	42	35	22	17		
Model 1	1.00 (ref.)	1.18 (0.75, 1.85)	1.11 (0.70, 1.76)	0.78 (0.45, 1.34)	0.51 (0.27, 0.94)	0.010	0.85 (0.71, 1.01)
Model 1 + BMI§	1.00 (ref.)	1.17 (0.75, 1.83)	0.95 (0.60, 1.50)	0.78 (0.46, 1.31)	0.63 (0.34, 1.17)	0.050	0.86 (0.72, 1.04)
Excluding participants with diabetes§§							
N Cases (score≥60)	35	40	35	22	16		
Model 1	1.00 (ref.)	1.06 (0.67, 1.66)	1.11 (0.71, 1.73)	0.74 (0.43, 1.27)	0.49 (0.26, 0.91)	0.009	0.84 (0.71, 0.998)
Model 1 + BMI§	1.00 (ref.)	1.06 (0.69, 1.65)	0.92 (0.59, 1.43)	0.76 (0.45, 1.29)	0.58 (0.32, 1.06)	0.033	0.85 (0.71, 1.02)
NAFLD-score ¶¶							
Different models							
N Cases (score≥-0.640)	41	46	51	38	32		
Multivariable (Model 1)‡	1.00 (ref.)	1.13 (0.75, 1.70)	1.26 (0.85, 1.87)	1.01 (0.65, 1.56)	0.80 (0.50, 1.28)	0.28	0.95 (0.82, 1.10)

Excluding alcohol from MD component							
Model 1 + Alcohol	1.00 (ref.)	1.15 (0.78, 1.71)	0.92 (0.61, 1.41)	0.92 (0.59, 1.42)	0.89 (0.57, 1.38)	0.34	0.93 (0.81, 1.08)
Model 1 + Alcohol + BMI§	1.00 (ref.)	1.15 (0.78, 1.69)	0.88 (0.59, 1.32)	0.88 (0.57, 1.35)	1.02 (0.66, 1.57)	0.65	0.96 (0.83, 1.12)
Excluding participants with BMI≥30‖							
N Cases (score≥-0.640)	40	46	44	36	31		
Model 1	1.00 (ref.)	1.15 (0.76, 1.74)	1.12 (0.74, 1.69)	0.99 (0.63, 1.55)	0.81 (0.5, 1.30)	0.27	0.94 (0.81, 1.09)
Model 1 + BMI§	1.00 (ref.)	1.17 (0.78, 1.75)	1.09 (0.73, 1.63)	1.07 (0.69, 1.67)	0.97 (0.6, 1.55)	0.76	0.99 (0.85, 1.15)
Excluding participants with excessive alcohol consumption**							
N Cases (score≥-0.640)	38	43	50	37	32		
Model 1	1.00 (ref.)	1.10 (0.73, 1.68)	1.28 (0.85, 1.91)	1.00 (0.64, 1.56)	0.80 (0.5, 1.29)	0.32	0.96 (0.83, 1.11)
Model 1 + BMI§	1.00 (ref.)	1.15 (0.76, 1.74)	1.18 (0.80, 1.73)	1.06 (0.69, 1.65)	0.96 (0.6, 1.54)	0.75	1.00 (0.86, 1.17)
Excluding participants with implausible energy intake††							
N Cases (score≥-0.640)	39	46	48	38	30		
Model 1	1.00 (ref.)	1.32 (0.75, 2.35)	1.48 (0.84, 2.60)	1.06 (0.59, 1.91)	1.15 (0.64, 2.07)	0.92	0.95 (0.82, 1.10)
Model 1 + BMI§	1.00 (ref.)	1.34 (0.76, 2.38)	1.35 (0.77, 2.37)	1.06 (0.59, 1.89)	1.29 (0.72, 2.33)	0.67	0.99 (0.85, 1.16)
Excluding participants with secondary causes of hepatic steatosis‡‡							
N Cases (score≥-0.640)	41	46	50	37	31		
Model 1	1.00 (ref.)	1.19 (0.79, 1.81)	1.26 (0.84, 1.89)	1.06 (0.68, 1.65)	0.78 (0.48, 1.27)	0.25	0.95 (0.82, 1.10)
Model 1 + BMI§	1.00 (ref.)	1.23 (0.82, 1.85)	1.17 (0.79, 1.73)	1.11 (0.71, 1.72)	0.93 (0.57, 1.52)	0.66	0.99 (0.85, 1.16)
Excluding participants with diabetes§§							
N Cases (score≥-0.640)	37	43	50	36	30		
Model 1	1.00 (ref.)	1.17 (0.76, 1.79)	1.37 (0.90, 2.06)	1.05 (0.67, 1.66)	0.85 (0.52, 1.39)	0.43	0.97 (0.83, 1.12)
Model 1 + BMI§	1.00 (ref.)	1.21 (0.79, 1.85)	1.26 (0.85, 1.87)	1.11 (0.71, 1.75)	1.01 (0.62, 1.63)	0.89	1.01 (0.86, 1.18)

Abbreviations: SES, socio economic status; BMI, body mass index; MD, Mediterranean Diet; NAFLD, non-alcoholic fatty liver disease; SD, standard deviation; CI, confidence interval.

Statistical analysis using Poisson regression with robust standard errors; results are expressed as risk ratios and (95% confidence intervals).

* In categorical analysis, the population was divided into five groups by quintiles (Q1-Q5) of the Mediterranean diet score; Standard deviation was 1.41 after excluding alcohol from Mediterranean Diet score components, 1.20 after excluding participants with BMI≥30, 1.18 after excluding participants with excessive alcohol consumption, 1.20 after excluding participants with probable implausible energy intake or after excluding participants with secondary causes of hepatic steatosis or diabetes.

† Calculated based on an algorithm including BMI, waist circumference, triglycerides, and gamma-glutamyl transferase.

‡ Adjusted for age (years), sex, marital status (single, married/cohabitant, and widowed/Separated/divorced), occupational status (working and not working), education level (university, high school, apprenticeship, and mandatory education), smoking status (never, former, and current), energy intake (kcal/day), total energy expenditure (kcal/day), and date of dietary assessment.

§ Results of further adjustment for waist circumference were broadly in line with of the further adjustment for BMI (data not shown).

‖ Excluded 36 participants with BMI≥30 kg/m^2.

** Excessive alcohol consumption defined as >21 units per week for men and >14 units per weeks for women; excluded 60 participants with excess alcohol consumption (n=2228).

†† Implausible energy intake defined as <500 and <800 kcal or >3,500 or >4,000 kcal in women and men, respectively; excluded 41 participants with probable implausible energy intake (n=2247).

‡‡ Secondary causes of hepatic steatosis defined as having hepatitis B, C or HIV, and with hepatotoxic medications (Glucocorticoids, isoniazid, methotrexate, amiodarone, and tamoxifen); excluded 36 participants with probable secondary causes of hepatic steatosis (n=2252).
§§ Diabetes defined as glycated haemoglobin≥48 mmol/mol, or fasting plasma glucose ≥7.0 mmol/L, or use of hypoglycaemic drugs or insulin; excluded 26 participants with probable secondary causes of hepatic steatosis (n=2262).
¶¶ Calculated based on an algorithm including presence of the metabolic syndrome and type 2 diabetes, and concentrations of fasting serum insulin, fasting serum aspartate-aminotransferase (AST), and the AST/alanine-aminotransferase ratio.

Table S5 Prospective association of the Mediterranean diet score with the risk of hepatic steatosis, CoLaus study, Switzerland: sensitivity analysis while excluding participants with only one of the indices high at baseline and using hepatic steatosis index as an alternative score.

	Risk ratio (95% CI) across quintiles of Mediterranean diet score*						
	Q1	Q2	Q3	Q4	Q5	*P*-trend	Risk ratio (95% CI) Per SD increase *
range	1.83-7.64	7.64-8.34	8.35-8.92	8.93-9.57	9.58-12.18		
N total (n=2652)	531	530	531	530	530		
Fatty liver index, *median* (iqr)†	23.4 (11.1, 41.4)	24.1 (10.6, 44.7)	22.3 (9.9, 39.7)	20.2 (8.4, 38.4)	17.5 (7.3, 34.5)		
N cases (score≥60)	51	56	54	35	24		
Unadjusted	1.00 (ref.)	1.10 (0.77, 1.58)	1.06 (0.74, 1.52)	0.69 (0.45, 1.04)	0.47 (0.29, 0.75)	<0.001	0.79 (0.69, 0.89)
Multivariable ‡	1.00 (ref.)	1.12 (0.77, 1.63)	1.25 (0.86, 1.81)	0.88 (0.57, 1.35)	0.56 (0.34, 0.92)	0.011	0.86 (0.74, 0.99)
Multivariable + BMI	1.00 (ref.)	1.08 (0.75, 1.54)	0.99 (0.70, 1.41)	0.85 (0.56, 1.30)	0.59 (0.36, 0.96)	0.017	0.84 (0.73, 0.98)
Multivariable + BMI & WC	1.00 (ref.)	1.01 (0.71, 1.45)	0.99 (0.70, 1.40)	0.84 (0.56, 1.28)	0.58 (0.35, 0.95)	0.019	0.84 (0.72, 0.98)
range	1.83-7.56	7.57-8.29	8.30-8.88	8.89-9.53	9.54-12.12		
N total (n=2568)	514	514	513	514	513		
NAFLD-score, *median* (iqr)§	-1.9 (-2.4, -1.3)	-1.8 (-2.3, -1.2)	-1.9 (-2.4, -1.3)	-2.0 (-2.5, -1.3)	-2.1 (-2.5, -1.6)		
N cases (score≥-0.640)	63	70	67	59	38		
Unadjusted	1.00 (ref.)	1.11 (0.81, 1.53)	1.07 (0.77, 1.47)	0.94 (0.67, 1.31)	0.60 (0.41, 0.89)	0.006	0.88 (0.79, 0.99)
Multivariable ‡	1.00 (ref.)	1.16 (0.83, 1.62)	1.16 (0.83, 1.61)	1.02 (0.72, 1.46)	0.66 (0.44, 1.00)	0.039	0.92 (0.81, 1.04)
Multivariable + BMI	1.00 (ref.)	1.27 (0.91, 1.76)	1.24 (0.89, 1.72)	1.16 (0.81, 1.65)	0.84 (0.55, 1.28)	0.34	0.98 (0.87, 1.11)
Multivariable + BMI & WC	1.00 (ref.)	1.25 (0.90, 1.73)	1.24 (0.89, 1.72)	1.16 (0.82, 1.65)	0.83 (0.54, 1.27)	0.34	0.99 (0.87, 1.12)
range	1.83-7.15	7.16-8.07	8.08-8.76	8.77-9.47	9.48-12.18		
N total (n=2351)	471	470	470	470	470		
Hepatic steatosis index, *median* (iqr)†	32.4 (30.5, 34.4)	32.3 (30.3, 34.6)	32.5 (30.4, 34.5)	32.6 (30.6, 34.4)	32.4 (30.3, 34.1)		
N cases (score>36)	166	123	120	120	103		
Unadjusted	1.00 (ref.)	0.74 (0.61, 0.90)	0.72 (0.59, 0.88)	0.72 (0.59, 0.88)	0.62 (0.50, 0.76)	<0.001	0.85 (0.79, 0.90)
Multivariable ‡	1.00 (ref.)	0.77 (0.61, 0.96)	0.79 (0.63, 1.00)	0.83 (0.65, 1.04)	0.70 (0.55, 0.91)	0.070	0.90 (0.82, 0.98)

Abbreviations: iqr, interquartile range; SES, socio-economic status; BMI, body mass index; WC, waist circumference; NAFLD, non-alcoholic fatty liver disease.
Statistical analysis using Poisson regression with robust standard errors; results are expressed as risk ratios and (95% confidence intervals).
* In categorical analysis, the population was divided into five groups by quintiles (Q1-Q5) of the Mediterranean diet score; Standard deviation was 1.21 for the multivariable analyses.
† Calculated based on an algorithm including BMI, waist circumference, triglycerides, and gamma-glutamyl transferase.
‡ Adjusted for age (years), sex, marital status (single, married/cohabiting, and widowed/Separated/divorced), occupational status (working and not working), education level (university, high school, apprenticeship, and mandatory education), smoking status (never, former, and current), energy intake (kcal/day), total energy expenditure (kcal/day), and date of dietary assessment.

§ Calculated based on an algorithm including presence of the metabolic syndrome and type 2 diabetes, and concentrations of fasting serum insulin, fasting serum aspartate-aminotransferase (AST), and the AST/alanine-aminotransferase ratio.

Table S6 Prospective association of the Mediterranean diet score with the risk of hepatic steatosis, CoLaus study, Switzerland (n=1632), Sensitivity analysis while excluding participants with either indices high (using FLI>30 instead of FLI≥60).

	Risk ratio (95% CI) across quintiles of Mediterranean diet score*					*P*-trend	Risk ratio (95% CI) Per SD increase*
	Q1	Q2	Q3	Q4	Q5		
range	1.83-7.63	7.64-8.35	8.36-8.92	8.93-9.59	9.60-12.1		
N total	327	326	327	326	326		
Fatty liver index, median (iqr)†	14.9 (7.6, 24.8)	12.7 (7.4, 23.7)	12.3 (5.5, 22.3)	11.8 (6.3, 22.7)	10.2 (5.5, 21.8)		
N cases (score≥60)	9	5	2	2	3		
Unadjusted	1.00 (ref.)	0.56 (0.19, 1.65)	0.22 (0.05, 1.02)	0.22 (0.05, 1.02)	0.33 (0.09, 1.22)	0.047	0.66 (0.45, 0.97)
Multivariable ‡	1.00 (ref.)	0.63 (0.20, 2.00)	0.14 (0.02, 0.96)	0.27 (0.05, 1.32)	0.39 (0.09, 1.68)	0.096	0.72 (0.47, 1.10)
Multivariable + BMI	1.00 (ref.)	0.68 (0.22, 2.05)	0.13 (0.02, 0.98)	0.26 (0.06, 1.15)	0.41 (0.10, 1.70)	0.087	0.73 (0.48, 1.11)
Multivariable + BMI + WC	1.00 (ref.)	0.50 (0.18, 1.42)	0.12 (0.01, 0.98)	0.22 (0.05, 1.03)	0.39 (0.09, 1.67)	0.093	0.71 (0.46, 1.09)
NAFLD-score, median (iqr)§	-2.2 (-2.5, -1.8)	-2.2 (-2.5, -1.7)	-2.2 (-2.5, -1.8)	-2.2 (-2.6, -1.8)	-2.2 (-2.6, -1.8)		
N cases (score≥-0.640)	13	14	10	13	12		
Unadjusted	1.00 (ref.)	1.08 (0.52, 2.26)	0.77 (0.34, 1.73)	1.00 (0.47, 2.13)	0.93 (0.43, 2.00)	0.79	0.94 (0.73, 1.20)
Multivariable ‡	1.00 (ref.)	1.13 (0.55, 2.32)	0.79 (0.35, 1.76)	1.10 (0.52, 2.34)	0.98 (0.45, 2.15)	0.94	0.95 (0.73, 1.24)
Multivariable + BMI	1.00 (ref.)	1.25 (0.60, 2.60)	0.81 (0.36, 1.84)	1.20 (0.56, 2.58)	1.13 (0.51, 2.52)	0.82	0.98 (0.75, 1.28)
Multivariable + BMI + WC	1.00 (ref.)	1.17 (0.57, 2.44)	0.85 (0.37, 1.93)	1.13 (0.52, 2.45)	1.12 (0.50, 2.53)	0.84	0.98 (0.75, 1.28)

Abbreviations: iqr, interquartile range; BMI, body mass index; WC, waist circumference; NAFLD, non-alcoholic fatty liver disease.
Statistical analysis using Poisson regression with robust standard errors; results are expressed as risk ratios and (95% confidence intervals).
* In categorical analysis, the population was divided into five groups by quintiles (Q1-Q5) of the Mediterranean diet score; Standard deviation was 1.21 for the multivariable analyses.
† Calculated based on an algorithm including BMI, waist circumference, triglycerides, and gamma-glutamyl transferase.
‡ Adjusted for age (years), sex, marital status (single, married/cohabiting, and widowed/Separated/divorced), occupational status (working and not working), education level (university, high school, apprenticeship, and mandatory education), smoking status (never, former, and current), energy intake (kcal/day), total energy expenditure (kcal/day), and date of dietary assessment.
§ Calculated based on an algorithm including presence of the metabolic syndrome and type 2 diabetes, and concentrations of fasting serum insulin, fasting serum aspartate-aminotransferase (AST), and the AST/alanine-aminotransferase ratio.

Table S7 Association of the Mediterranean diet score with change in BMI and waist circumference, CoLaus study, Switzerland.

	β coefficient (95% CI) across quintiles of Mediterranean diet score*					*P*-trend	β coefficient (95% CI) Per SD increase*
	Q1	Q2	Q3	Q4	Q5		
range	1.83-7.63	7.64-8.35	8.36-8.92	8.93-9.59	9.60-12.1		
N total	458	458	457	458	457		
ΔBMI, mean±SD†	0.48 ± 1.62	0.61 ± 1.53	0.42 ± 1.44	0.50 ± 1.52	0.40 ± 1.52		
Multivariable ‡	1.00 (ref.)	0.12 (-0.08, 0.33)	-0.08 (-0.28, 0.13)	-0.04 (-0.25, 0.16)	-0.16 (-0.37, 0.04)	0.038	-0.08 (-0.15, -0.02)
ΔWaist circumference, mean±SD§	1.04 ± 6.53	0.74 ± 6.42	0.19 ± 6.00	0.57 ± 6.33	0.17 ± 6.19		
Multivariable ‡	1.00 (ref.)	-0.51 (-1.36, 0.34)	-0.85 (-1.69, 0.00)	-0.47 (-1.32, 0.38)	-0.82 (-1.68, 0.03)	0.10	-0.33 (-0.61, -0.06)

Abbreviations: BMI, Body mass index.

Statistical analysis using linear regression; results are expressed as β coefficients and (95% confidence intervals).

* In categorical analysis, the population was divided into five groups by quintiles (Q1-Q5) of the Mediterranean diet score; Standard deviation was 1.20 for the multivariable analyses.

† Calculated by subtracting BMI at baseline from BMI at follow-up.

‡ Adjusted for age (years), sex, marital status (single, married/cohabitant, and widowed/Separated/divorced), occupational status (working and not working), education level (university, high school, apprenticeship, and mandatory education), smoking status (never, former, and current), energy intake (kcal/day), total energy expenditure (kcal/day), and date of dietary assessment.

§ Calculated by subtracting waist circumference at baseline from waist circumference at follow-up.

Table S8 Association of the Mediterranean diet score with the GGT, ALT, and AST, CoLaus study, Switzerland.

	β coefficient (95% CI) across quintiles of Mediterranean diet score*					*P*-trend	β coefficient (95% CI) Per SD increase *
	Q1	Q2	Q3	Q4	Q5		
range	1.83-7.63	7.64-8.35	8.36-8.92	8.93-9.59	9.60-12.12		
N total	458	458	457	458	457		
GGT (U/l), *median* (iqr)	21 (15, 29)	20 (14, 29)	19 (14, 26)	18 (14, 28)	17 (13, 26)		
Multivariable †	1.00 (ref.)	-2.63 (-9.01, 3.76)	-5.71 (-12.07, 0.66)	-4.24 (-10.64, 2.16)	-6.03 (-12.45, 0.38)	0.063	-1.53 (-3.60, 0.53)
Multivariable + BMI	1.00 (ref.)	-2.86 (-9.24, 3.53)	-5.70 (-12.06, 0.66)	-4.50 (-10.90, 1.90)	-6.52 (-12.95, -0.09)	0.047	-1.66 (-3.73, 0.41)
Multivariable + BMI & WC	1.00 (ref.)	-2.93 (-9.32, 3.45)	-5.72 (-12.08, 0.64)	-4.54 (-10.94, 1.86)	-6.53 (-12.96, -0.10)	0.047	-1.65 (-3.72, 0.41)
ALT (U/l), *median* (iqr)	20 (16, 26)	20.5 (17, 26)	20 (16, 26)	19.5 (16, 25)	20 (16, 25)		
Multivariable †	1.00 (ref.)	0.03 (-0.02, 0.08)	0.03 (-0.02, 0.08)	-0.013 (-0.06, 0.04)	0.002 (-0.05, 0.05)	0.45	-0.006 (-0.02, 0.01)
Multivariable + BMI	1.00 (ref.)	0.04 (-0.01, 0.08)	0.03 (-0.02, 0.08)	-0.009 (-0.06, 0.04)	0.008 (-0.04, 0.06)	0.60	-0.005 (-0.02, 0.01)
Multivariable + BMI & WC	1.00 (ref.)	0.04 (-0.01, 0.08)	0.03 (-0.02, 0.08)	-0.01 (-0.06, 0.04)	0.008 (-0.04, 0.06)	0.60	-0.005 (-0.02, 0.01)
AST (U/l), *median* (iqr)	22 (19, 25)	22 (19, 26)	22 (19, 25)	22 (19, 26)	22 (19, 25)		
Multivariable †	1.00 (ref.)	0.02 (-0.01, 0.06)	0.004 (-0.03, 0.04)	0.011 (-0.03, 0.05)	0.015 (-0.02, 0.05)	0.66	0.003 (-0.01, 0.01)
Multivariable + BMI	1.00 (ref.)	0.02 (-0.02, 0.06)	0.004 (-0.03, 0.04)	0.009 (-0.03, 0.04)	0.011 (-0.03, 0.05)	0.80	0.002 (-0.01, 0.01)
Multivariable + BMI & WC	1.00 (ref.)	0.02 (-0.02, 0.06)	0.004 (-0.03, 0.04)	0.009 (-0.03, 0.04)	0.011 (-0.03, 0.05)	0.80	0.002 (-0.01, 0.01)

Abbreviations: iqr, interquartile range; GGT, gamma-glutamyl transferase; SES, socio economic status; BMI, body mass index; WC, waist circumference; ALT, Alanine transaminase; AST, aspartate-aminotransferase.

Statistical analysis using linear regression; results are expressed as β coefficients and (95% confidence intervals).

* In categorical analysis, the population was divided into five groups by quintiles (Q1-Q5) of the Mediterranean diet score; Standard deviation was 1.20 for the multivariable analyses.

† Adjusted for age (years), sex, marital status (single, married/cohabitant, and widowed/Separated/divorced), occupational status (working and not working), education level (university, high school, apprenticeship, and mandatory education), smoking status (never, former, and current), energy intake (kcal/day), total energy expenditure (kcal/day), and date of dietary assessment.