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Meat and fish consumption, genetic risk and risk of severe metabolic-associated fatty liver disease: a prospective cohort of 487,875 individuals

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Abstract

Background Diet, specifically meat consumption, has been implicated as a modifiable risk factor in the development of metabolic-associated fatty liver disease (MAFLD). This study aimed to investigate the associations between various types of meat intake and the risk of severe MAFLD and to examine whether genetic risk influences these associations.

Methods This research utilized data from the UK Biobank, which initially enrolled over 500,000 participants between 2006 and 2010, of whom 487,875 were eligible for our analyses. Meat intake, including unprocessed red meat, processed meat, poultry, and fish, was evaluated through a validated touchscreen questionnaire. Cox proportional hazards models were used to analyze the relationship between meat consumption and severe MAFLD risk, adjusting for potential confounders. Genetic risk scores (GRS) were calculated using five MAFLD-associated SNPs, allowing for analyses of gene-diet interactions.

Results During a follow-up period totaling 6,036,554 person-years (mean duration: 12.1 years), 5,731 new cases of severe MAFLD were identified. High intakes of total meat, processed meat, unprocessed red meat and poultry were associated with increased MAFLD risk, with adjusted hazard ratios (HR) of 1.76 (95% CI: 1.33–2.33), 1.19 (1.02–1.40), 1.34 (1.17–1.53), and 1.21 (0.98–1.49), respectively, for the highest versus lowest intake categories. In contrast, oily fish intake showed a protective association (HR: 0.72; 95% CI: 0.53–0.97). No significant interaction was observed between meat intake and GRS for any meat subtype, suggesting that the associations were independent of genetic predisposition.

Conclusions High consumption of red and processed meat was associated with an increased risk of severe MAFLD, while oily fish intake showed an inverse association with the risk of MAFLD. These effects were consistent across

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genetic risk levels for MAFLD. Our findings reinforce dietary recommendations to limit red and processed meat and encourage oily fish intake for MAFLD prevention, irrespective of individual genetic risk.

Keywords Non-alcoholic fatty liver disease, Meat consumption, Genetic risk, Cohort study, Genetic risk score

Introduction

Metabolic-associated fatty liver disease (MAFLD) has emerged as the most prevalent chronic liver disease globally, affecting an estimated 25% of the adult population [1]. MAFLD can advance to cirrhosis and hepatocellular carcinoma, representing a leading cause of liver-related mortality worldwide. Due to the increasing prevalence of metabolic risk factors and the aging population globally, the burden of advanced stages of MAFLD and its associated economic impact are anticipated to increase substantially [2–4].

The pathogenesis of MAFLD is understood to be influenced by the interplay between genetic predispositions and lifestyle factors [5]. Dietary composition plays a crucial role, with excessive intake of refined carbohydrates, saturated fats, and ultra-processed foods promoting hepatic fat accumulation and inflammation [6]. In the absence of established pharmacological treatments for MAFLD, it is essential to identify modifiable risk factors that may aid in prevention and potentially slow disease progression [7]. Dietary habits, particularly meat consumption (including total meat, processed meat, unprocessed red meat, poultry, and fish), have been identified as modifiable risk factors associated with MAFLD development [8–10]. High consumption of red and processed meats has been linked to insulin resistance and an increased risk of MAFLD [11, 12]. However, some studies indicate that, after adjusting for multiple confounders, neither unprocessed nor processed red meat shows a direct association with MAFLD risk [13–15]. Similarly, other studies have found no detrimental association between processed meat and MAFLD risk [16, 17]. With regard to fish consumption, its relationship with MAFLD risk at the population level remains inconclusive; while some prospective studies suggest a protective role [16, 18], others report no significant association [19–21]. Evidence on poultry consumption and MAFLD risk is also limited and yields inconsistent results [15, 22]. Notably, most available evidence is based on cross-sectional studies with small sample sizes, highlighting the need for further large-scale, prospective research to elucidate the long-term effects of meat consumption on MAFLD development.

In recent years, large-scale genome-wide association studies (GWAS) have identified genetic loci associated with MAFLD risk, including variants in genes such as PNPLA3, TM6SF2, and GCKR [23]. Using these genetic variants, researchers can construct a polygenic risk score to quantify genetic susceptibility, which facilitates the study of gene-diet interactions [24]. Dietary factors, including meat consumption, are hypothesized to interact with genetic predispositions to influence MAFLD development [25]. However, evidence on these interactions remains limited. Investigating how different types of meat consumption interact with genetic risk to impact MAFLD incidence may provide insights that inform precision nutrition approaches.

The study had two primary objectives: first, to examine the association between various types of meat consumption and the incidence of severe MAFLD, and second, to evaluate the interactions between meat intake and genetic risk in the development of MAFLD.

Methods

Population

The UK Biobank is a large-scale prospective cohort study that recruited over 500,000 participants aged 37 to 73 years at baseline from diverse regions across the United Kingdom. From 2006 to 2010, participants attended one of 22 assessment centers, where they underwent comprehensive physical measurements, provided biological samples, and completed detailed touchscreen questionnaires. Ethical approval for the UK Biobank study was granted by the North West Multi-centre Research Ethics Committee [26].

For this analysis, the UK Biobank dataset included 502,406 participants. We excluded individuals who subsequently withdrew, those diagnosed with MAFLD or other liver diseases prior to study entry, participants with a history of substance abuse or alcoholism at baseline, and those lacking data on meat intake. A total of 484,875 participants remained eligible for the analysis of associations between meat consumption and MAFLD incidence. For the gene-diet interaction analysis, we further restricted the sample to individuals of white British descent with available genetic data, yielding a final sample of 364,619 participants for this analysis (Fig. 1).

Meat intake and covariates

The intake of various types of meat, including unprocessed red meat, processed meat, oily fish, non-oily fish, beef, lamb, pork, and poultry, was assessed through a touchscreen-based short food frequency questionnaire (FFQ) covering the past 12 months. Meat intake frequencies were categorized as never, <1 time/week, 1 time/week, 2–4 times/week, 5–6 times/week, or ≥7 times/week. Total meat consumption was calculated by summing the intake frequencies of unprocessed red meat

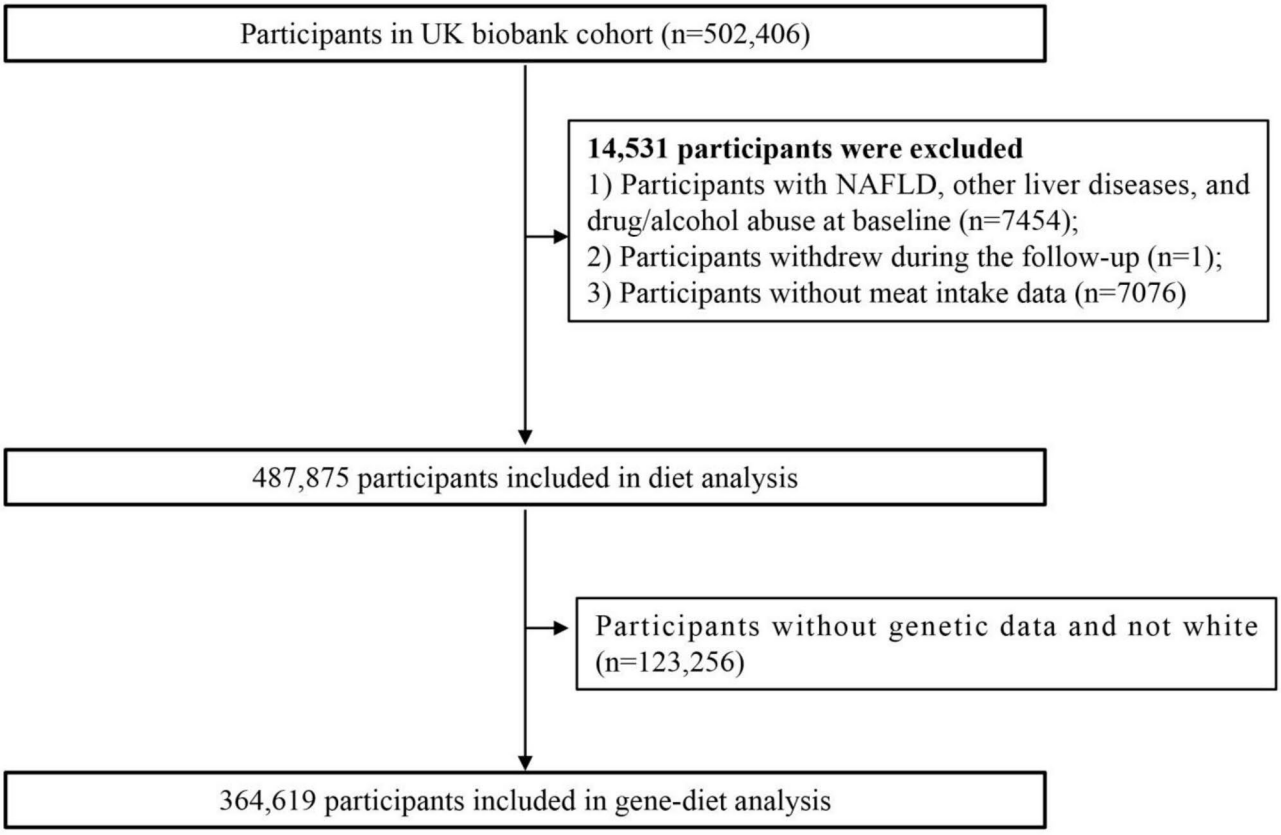

Fig. 1 Flow of participants in current UK biobank study

(beef, lamb, and pork), unprocessed poultry, processed meat (bacon, ham, sausages, meat pies, kebabs, burgers, and chicken nuggets), oily fish, and non-oily fish. The short FFQ has been validated against 24-hour dietary recalls. Diet quality was assessed using the Alternate Mediterranean Diet (AMED) score, which ranged from 0 to 9, with higher scores indicating better diet quality, as previously described [27]. Healthy diet score includes 10 foods predictive of cardiometabolic disease risk, emphasizing higher intake of vegetables, fruits, fish, dairy, whole grains, and vegetable oils and lower intake of refined grains, processed meats, unprocessed red meats, and sugar-sweetened beverages [28]. Each dietary component was scored from 0 (unhealthiest) to 10 (healthiest) points, with intermediate values scored proportionally. The total diet quality score was the sum of all the diet component scores and ranged from 0 to 100, with a higher score representing a higher overall diet quality. The UK Biobank also utilized the Oxford WebQ, a web-based 24-hour recall questionnaire administered on five occasions, to collect dietary data between 2009 and 2012. The average dietary intake was calculated using all available assessments to represent long-term dietary intake.

Potential confounding factors were collected via touchscreen questionnaire, including age, sex, ethnicity, weight, height, income, education level, smoking and drinking habits, physical activity, Townsend deprivation index [29], and medical history. The metabolic equivalent of task (MET) was calculated using the short form of the International Physical Activity Questionnaire [30].

Genetic risk score for MAFLD

Genotyping considerations, quality control, and genetic imputation details have been described previously [26]. We selected five single nucleotide polymorphisms (SNPs)—rs738409, rs58542926, rs641738, rs1260326, and rs72613567 (Table S1)—associated with MAFLD risk, based on prior MAFLD cohort analyses. The genetic risk score (GRS) was calculated using these SNPs, with corresponding β coefficients applied in the following formula: $GRS = (\beta_1 \times SNP_1 + \beta_2 \times SNP_2 + . + \beta_i \times SNP_i) \times (i / \text{sum of the } \beta \text{ coefficients})$ [31], where β represents the coefficient for each SNP, and i indicates the number of risk alleles for each SNP. A higher GRS reflects greater genetic susceptibility to MAFLD.

Definition of severe MAFLD

In this study, severe MAFLD was defined as hospitalization or death due to MAFLD or non-alcoholic steatohepatitis (NASH), based on linked hospitalization and

mortality databases. Hospitalization data, including dates and diagnoses, were obtained from hospital episode statistics, covering participants in England and Wales until September 30, 2021, and in Scotland until September 24, 2021. Severe MAFLD was identified using the International Classification of Diseases, 10th Revision (ICD-10) codes K76.0 (fatty liver, not elsewhere classified) and K75.8 (NASH, other specified inflammatory liver diseases) [32]. The follow-up period was calculated from the date of recruitment to the earliest of the following events: first diagnosis of severe MAFLD, death, loss to follow-up, or the end of the study on November 12, 2021.

Statistical analysis

Continuous variables are presented as mean ± standard deviation, and categorical variables are presented as percentages. To examine the association between meat consumption (assessed by short FFQ) and the risk of severe MAFLD, we used Cox proportional hazards models, categorizing meat intake into groups: never, 0–3 times/week, 3–5 times/week, 5–7 times/week, or ≥7 times/week (C1 to C5), with the lowest category as the reference group. The proportional hazards assumption was validated using Schoenfeld residuals, and results were expressed as hazard ratios (HR) with 95% confidence intervals (CI). Sequential models were adjusted for confounders identified in previous studies: Model 1 included adjustments for age (continuous) and sex (men or women); Model 2 further adjusted for ethnicity (white, Asian, black, mixed, or other ethnic group), assessment center location, BMI (in kg/m^2; <18.5, 18.5 to 25, 25 to 30, ≥30, or missing), education level (college or university degree, vocational qualifications, optional national exams at ages 17–18 years, national exams at age 16 years, others, or missing), household income (<£18,000, £18,000-£30,999, £31,000-£51,999, £52,000-£100,000, >£100,000, or missing), smoking status (never, former, current, or missing), alcohol consumption (never or special occasions only, 1 to 3 times/month, 1 or 2 times/week, 3 or 4 times/week, or daily/almost daily), physical activity (quartiles), and the Townsend deprivation index (quartiles); Model 3 additionally controlled for intake of other meat types (unprocessed red meat, processed meat, unprocessed poultry, oily fish, and non-oily fish; categorical), vegetables (0 to 1 times/day, 1 to 3 times/day, more than 3 times/day), fruits (0 to 2 times/day, 2 to 4 times/day, more than 4 times/day), and total energy intake (quartiles); Model 4 included adjustments in Model 2 as well as additional controls for other meat types (5 categories), total energy intake (quartiles), and AMED score (total score minus the component for meat; quartiles). Missing data were managed by creating a missing indicator category where applicable. Additionally, to enhance the accuracy of dietary assessment and complement the analysis based on frequency, we incorporated food weight, which provides a more precise quantification of intake and reduces potential misclassification. Using variables from 24-hour dietary recalls reflecting mean intake in grams per day (g/d), we further examined the association between meat consumption and the risk of MAFLD based on food weight ($n = 207,465$).

To assess the interaction between meat intake and MAFLD GRS, we included a multiplicative interaction term in the Cox models. Further categorical analyses were conducted to determine whether HRs for a 1-standard deviation increase in meat consumption varied across tertiles of GRS. Subgroup analyses stratified by baseline characteristics were performed to evaluate the impact of covariate variations on associations. Sensitivity analyses included additional adjustments for lipid-lowering medication use and replacement of the AMED score with a healthy diet score, and exclusion of incident MAFLD cases diagnosed within the first five years of follow-up to minimize reverse causality.

All analyses were conducted using SAS 9.4 (SAS Institute, Cary, NC, USA), and a p-value of less than 0.05 was considered statistically significant.

Results

Baseline characteristics of study participants

In this study, total meat intake was classified into five categories based on weekly consumption frequency: 0 times/week, 0.1-3 times/week, 3.1–4.9 times/week, 5.0-6.9 times/week, and ≥7 times/week. Baseline characteristics were examined across these groups, revealing variations in demographic, socioeconomic, and health-related factors (Table 1). Participants with higher total meat intake were more likely to be male, older, and have a higher BMI. This group was predominantly White, had higher household incomes, was more likely to be former smokers, and reported more frequent alcohol consumption. Additionally, individuals with higher meat intake tended to have lower levels of education and reported greater consumption of unprocessed red meat, processed meat, and poultry.

Relationship between meat consumption and severe MAFLD risk

Over a follow-up period totaling 6,036,554 person-years, with an average duration of 12.1 years per participant, 5,731 new cases of severe MAFLD were identified. The analysis demonstrated a consistent and significant association between frequent consumption of total meat, processed meat, and unprocessed red meat and an increased risk of severe MAFLD. This association was observed in both age- and sex-adjusted models (Model 1) and in multivariable-adjusted models (Model 2, which controlled for demographic and lifestyle factors; Model 3, which

Table 1 Baseline characteristics of participants by categories of total meat intake in the UK biobank cohort

Characteristics	Total meat intake (times/week)				
	0 times/week	0.1-3 times/week	3.1–4.9 times/week	5.0-6.9 times/week	≥ 7 times/week
N	9032	16,027	47,662	112,973	302,181
Age (year)	53.24 ± 7.95[a]	54.67 ± 8.06	56.41 ± 8.02	56.69 ± 8.01	56.70 ± 8.10
Male (%)	33.26	29.74	36.47	40.07	49.65
Ethnicity (%)					
White	79.71	89.08	94.23	95.30	95.00
Non-white	19.62	10.41	5.45	4.39	4.67
BMI (kg/m^2)	25.69 ± 4.66	25.99 ± 4.78	26.65 ± 4.62	27.13 ± 4.67	27.76 ± 4.81
Townsend deprivation index	-0.68 ± 3.09	-0.58 ± 3.24	-1.13 ± 3.09	-1.41 ± 3.01	-1.43 ± 3.05
Physical activity (MET-h/wk)	45.68 ± 43.84	44.22 ± 44.11	43.38 ± 43.82	43.31 ± 43.99	45.43 ± 47.81
Household income (£) (%)[b]					
< 18,000	18.46	23.84	21.51	19.32	18.22
18,000 to 30,999	19.84	20.76	22.14	21.86	21.65
31,000 to 51,999	23.85	21.43	21.43	22.22	22.55
52,000 to 100,000	19.03	15.52	16.11	17.14	17.89
> 100,000	3.94	3.43	3.81	4.40	4.99
Education					
College or University degree	49.21	41.44	34.76	32.02	31.39
Others	48.68	56.78	63.55	66.30	66.85
Smoking (%)					
Never	63.82	57.14	55.84	55.80	54.11
Previous	29.00	31.75	33.46	34.05	35.24
Current	6.73	10.69	10.32	9.80	10.32
Alcohol drinking (%)					
Never or special occasions only	38.26	33.46	23.58	20.28	16.90
1 to 3 times/month	11.66	13.51	13.16	12.09	10.41
1 or 2 times/week	19.35	22.81	26.17	26.87	25.89
3 or 4 times/week	17.09	16.58	20.16	21.97	24.73
Daily or almost daily	13.46	13.52	16.86	18.73	22.01
Energy intake	2014.46 ± 636.13	1941.56 ± 605.94	1965.79 ± 565.92	2005.59 ± 577.05	2111.53 ± 612.64
Unprocessed red meat (times/week)	0.00 ± 0.00	0.38 ± 0.52	1.26 ± 0.60	1.69 ± 0.77	2.56 ± 1.55
Processed meat (times/week)	0.00 ± 0.00	0.25 ± 0.35	0.58 ± 0.40	0.92 ± 0.78	1.94 ± 1.50
Unprocessed poultry (times/week)	0.00 ± 0.00	0.39 ± 0.40	0.81 ± 0.51	1.46 ± 0.99	2.41 ± 1.18
Oily fish (times/week)	0.00 ± 0.00	0.50 ± 0.41	0.71 ± 0.62	0.84 ± 0.72	1.35 ± 1.16
Non-oily fish (times/week)	0.00 ± 0.00	0.60 ± 0.38	0.76 ± 0.52	0.89 ± 0.60	1.38 ± 1.04

BMI body mass index, *MET* metabolic equivalent of task

[a]Data are either percentage or mean (SD) unless indicated otherwise

[b]£1.00=$1.30, €1.20

additionally adjusted for intake of other food types), as shown in Table 2. In the final model, which further adjusted for total dietary energy intake and the AMED score (Model 4), the association remained unchanged. Specifically, participants in the highest category of total meat intake exhibited a 76% higher risk of MAFLD compared to those in the lowest category (HR: 1.76; 95% CI: 1.33–2.33; P for trend < 0.001). Processed meat consumption was associated with a 19% increased risk (HR: 1.19; 95% CI: 1.02–1.40; P for trend = 0.003), and unprocessed red meat intake was associated with a 34% increased risk (HR: 1.34; 95% CI: 1.17–1.53; P for trend < 0.001) when comparing the highest and lowest consumption categories. Unprocessed poultry consumption was also associated with a higher MAFLD risk (HR for highest vs. lowest category: 1.21; 95% CI: 0.98–1.49; P for trend < 0.001). In contrast, oily fish intake showed an inverse association with severe MAFLD risk (P for trend = 0.033), with a multivariable-adjusted (Model 4) HR of 0.72 (95% CI: 0.53–0.97) for the highest versus lowest intake category. No association was observed for non-oily fish consumption. Additionally, we also assessed the association between meat intake and MAFLD risk based on food intake in "g/d" rather than frequency and showed essentially similar results (Table S2). Total meat and processed meat consumption were positively associated with MAFLD risk, whereas the inverse association

Table 2 Associations between meat intake and MAFLD risk

Meat types	Meat intake (times/week)					*P* trend
	C1	C2	C3	C4	C5	
Total meat						
Frequency	0 times/week	0.1-3 times/week	3.1–4.9 times/week	5.0-6.9 times/week	≥ 7 times/week	
Case/person-years	50/111,230	165/197,337	514/585,898	1192/1,389,565	3731/3,706,788	
Model 1[a]	1 (ref)	1.82 (1.33–2.50)	1.87 (1.40–2.50)	1.82 (1.37–2.41)	2.13 (1.61–2.82)	< 0.001
Model 2[b]	1 (ref)	1.65 (1.20–2.27)	1.70 (1.27–2.28)	1.62 (1.22–2.15)	1.80 (1.36–2.39)	< 0.001
Model 3[c]	1 (ref)	1.62 (1.18–2.22)	1.67 (1.25–2.24)	1.60 (1.20–2.13)	1.79 (1.35–2.37)	< 0.001
Model 4[d]	1 (ref)	1.63 (1.18–2.23)	1.67 (1.25–2.23)	1.58 (1.19–2.11)	1.76 (1.33–2.33)	< 0.001
Unprocessed red meat						
Frequency	0 times/week	0.1–0.9 times/week	1 times/week	2.0-4.9 times/week	≥ 5 times/week	
Case/person-years	410/568,181	1582/1,854,381	1682/1,766,145	1773/1,616,499	284/231,348	
Model 1[a]	1 (ref)	1.52 (1.32–1.76)	1.38 (1.21–1.58)	1.45 (1.27–1.65)	1.70 (1.49–1.94)	< 0.001
Model 2[b]	1 (ref)	1.23 (1.07–1.42)	1.24 (1.09–1.42)	1.29 (1.13–1.47)	1.40 (1.22–1.60)	< 0.001
Model 3[c]	1 (ref)	1.19 (1.03–1.38)	1.21 (1.06–1.39)	1.25 (1.09–1.43)	1.35 (1.18–1.55)	< 0.001
Model 4[d]	1 (ref)	1.19 (1.03–1.37)	1.20 (1.05–1.38)	1.24 (1.08–1.42)	1.34 (1.17–1.53)	< 0.001
Processed meat						
Frequency	0 times/week	0.1-1.0 times/week	1.1–1.9 times/week	2.0-2.9 times/week	≥ 3 times/week	
Case/person-years	265/413,994	710/723,175	1673/1,873,376	1592/1,688,420	1491/1,337,591	
Model 1[a]	1 (ref)	1.16 (1.04–1.29)	1.31 (1.17–1.46)	1.53 (1.37–1.71)	1.74 (1.49–2.03)	< 0.001
Model 2[b]	1 (ref)	1.08 (0.97–1.21)	1.13 (1.02–1.27)	1.19 (1.06–1.33)	1.26 (1.08–1.48)	< 0.001
Model 3[c]	1 (ref)	1.05 (0.94–1.18)	1.09 (0.97–1.22)	1.13 (1.01–1.27)	1.18 (1.01–1.39)	0.005
Model 4[d]	1 (ref)	1.05 (0.94–1.17)	1.09 (0.97–1.22)	1.13 (1.01–1.27)	1.19 (1.02–1.40)	0.003
Unprocessed poultry						
Frequency	0 times/week	0.1–0.9 times/week	1 times/week	2.0-4.9 times/week	≥ 5 times/week	
Case/person-years	206/309,876	570/642,438	1976/2,163,341	2811/2,784,143	168/136,757	
Model 1[a]	1 (ref)	1.27 (1.08–1.49)	1.31 (1.13–1.51)	1.48 (1.28–1.70)	1.88 (1.53–2.30)	< 0.001
Model 2[b]	1 (ref)	1.12 (0.95–1.31)	1.19 (1.03–1.38)	1.27 (1.10–1.46)	1.27 (1.03–1.56)	< 0.001
Model 3[c]	1 (ref)	1.09 (0.93–1.28)	1.16 (1.00-1.35)	1.24 (1.07–1.44)	1.22 (0.99–1.50)	< 0.001
Model 4[d]	1 (ref)	1.09 (0.93–1.28)	1.15 (1.00-1.34)	1.22 (1.06–1.42)	1.21 (0.98–1.49)	< 0.001
Oily fish						
Frequency	0 times/week	0.1–0.9 times/week	1 times/week	2.0-4.9 times/week	≥ 5 times/week	
Case/person-years	778/651,024	1908/1,988,244	1966/2,271,614	955/1,023,816	45/56,120	
Model 1[a]	1 (ref)	0.79 (0.72–0.86)	0.69 (0.64–0.75)	0.74 (0.67–0.81)	0.64 (0.47–0.87)	< 0.001
Model 2[b]	1 (ref)	0.95 (0.87–1.03)	0.91 (0.83–0.99)	0.94 (0.85–1.03)	0.72 (0.54–0.98)	0.044
Model 3[c]	1 (ref)	0.95 (0.87–1.03)	0.91 (0.84–0.99)	0.94 (0.85–1.04)	0.72 (0.53–0.98)	0.071
Model 4[d]	1 (ref)	0.94 (0.86–1.02)	0.90 (0.82–0.98)	0.93 (0.84–1.03)	0.72 (0.53–0.97)	0.033
Non-oily fish						
Frequency	0 times/week	0.1–0.9 times/week	1 times/week	2.0-4.9 times/week	≥ 5 times/week	
Case/person-years	289/278,193	1657/1,738,454	2751/2,989,910	921/946,735	34/37,525	
Model 1[a]	1 (ref)	0.89 (0.79–1.01)	0.85 (0.75–0.96)	0.90 (0.79–1.03)	0.86 (0.60–1.23)	0.177
Model 2[b]	1 (ref)	0.96 (0.85–1.09)	0.98 (0.87–1.11)	1.00 (0.87–1.14)	0.83 (0.59–1.19)	0.730
Model 3[c]	1 (ref)	0.94 (0.83–1.07)	0.96 (0.85–1.09)	0.97 (0.85–1.11)	0.80 (0.56–1.14)	0.950
Model 4[d]	1 (ref)	0.94 (0.83–1.07)	0.95 (0.84–1.07)	0.96 (0.84–1.10)	0.80 (0.56–1.14)	0.750

CI confidence interval, *HR* hazard ratio, *MAFLD* metabolic-associated fatty liver disease

[a]Model 1 was adjusted for age and sex

[b]Model 2 was further adjsted for ethnicity (white, Asian, black, mixed, or other ethnic group), centers (22 categories), BMI (in kg/m2; <18.5, 18.5 to 25, 25 to 30, 30 to 35, ≥ 35, or missing), education (college or university degree, vocational qualifications, optional national exams at ages 17–18 years, national exams at age 16 years, others, or missing), Townsend deprivation index (quartiles), household income (<£18,000, £18,000-£30,999, £31,000-£51,999, £52,000-£100,000, >£100,000, or missing), smoking (never, former, current, or missing), alcohol consumption (never or special occasions only, 1 to 3 times/month, 1 or 2 times/week, 3 or 4 times/week, or daily/almost daily), physical activity (in MET-h/wk; quartiles)

[c]Model 3 was further adjusted for other remaining meats (unprocessed red meat, processed meat, unprocessed poultry, oily fish and non-oily fish), vegetable, fruit, and total energy intake

[d]Model 4 was further adjusted for model 2 plus other remaining meats (unprocessed red meat, processed meat, unprocessed poultry, oily fish and non-oily fish), total energy intake, and Alternate Mediterranean Diet score (total score minus the meat component)

between fish intake and MAFLD remained but did not reach statistical significance.

Interactions of different types of meat with MAFLD genetic risk

Table 3 presents the interactions between meat intake and the GRS for MAFLD. The analysis revealed a positive association between total meat intake and MAFLD risk, with a significant β of 0.074 (SE: 0.018, $P<0.001$). Both unprocessed red meat and unprocessed poultry showed similar associations with MAFLD risk (β = 0.067 and 0.058, respectively, both $P<0.001$). However, no significant interaction was found between meat intake and GRS for any meat subtype (all P interaction > 0.05).

In a categorical analysis, we further evaluated the HR of MAFLD associated with different meat types, stratified by tertiles of genetic risk (low, normal, and high risk). Total meat, unprocessed red meat, and unprocessed poultry intake were consistently associated with a higher MAFLD risk across tertiles of genetic risk (Fig. 2). Conversely, oily fish intake was inversely associated with MAFLD risk among those with normal or high genetic risk, with HRs not significantly different across tertiles of GRS. Overall, no significant interactions between subtypes of meat and tertiles of GRS for MAFLD were detected (all $P>0.05$). These findings suggest that the relationship between meat intake and MAFLD is largely independent of genetic predisposition.

Subgroup analysis

Subgroup analyses revealed notable variations in the association between meat intake and the risk of severe MAFLD (Table S3). Specifically, the positive association between total meat intake and severe MAFLD risk was more pronounced among participants under 60 years of age (P for interaction < 0.001) and those without a history of diabetes or hypertension (P for interaction < 0.001). Additionally, the association between unprocessed red meat intake and severe MAFLD was stronger in participants under 60, current smokers, and those without a history of diabetes or hypertension (all P for interaction < 0.001). For processed meat, the risk increase was particularly marked among participants under 60 and those without a history of diabetes or hypertension (all P for interaction < 0.001). Conversely, higher oily fish intake was inversely associated with MAFLD risk across various subgroups, with a more pronounced association observed among older adults and those without diabetes or with hypertension (all P for interaction < 0.001).

Sensitivity analysis

Sensitivity analyses further confirmed the robustness of the associations between meat intake and the risk of severe MAFLD (Table S4). After adjusting for lipid-lowering medication use, total meat, unprocessed red meat, processed meat, and unprocessed poultry remained significantly associated with an increased risk of MAFLD. Adjusting for a healthy diet score (instead of an AMED score) produced similar results, particularly for total meat and unprocessed red meat intake. When excluding MAFLD cases that developed within the first five years of follow-up to minimize reverse causality, the positive associations persisted, reinforcing the strength of these findings. Oily fish intake continued to show an inverse association.

Discussion

In this extensive cohort study involving 487,875 individuals, we observed a significant association between high meat consumption and an increased risk of severe MAFLD. High intake of total meat, processed meat, and unprocessed red meat was linked to a higher risk of severe MAFLD, whereas oily fish consumption was associated with a reduced risk. Importantly, these associations were not modified by the genetic risk of MAFLD.

Previous studies have reported inconsistent associations between unprocessed red meat intake and the incidence of MAFLD [10, 14, 15, 22], possibly due to differences in the definition of red meat, variations in intake standards, limited sample sizes, or insufficient follow-up

Table 3 Interactions of meat intake with GRS for MAFLD

	Meat intake			GRS for MAFLD			Meat intake × GRS		
	β[a]	SE	*P*	β[a]	SE	*P*	β[a]	SE	*P*
Total meat	0.074	0.018	< 0.001	0.149	0.016	< 0.001	-0.002	0.018	0.928
Unprocessed red meat	0.067	0.015	< 0.001	0.147	0.016	< 0.001	0.016	0.015	0.275
Unprocessed poultry	0.058	0.016	< 0.001	0.149	0.016	< 0.001	0.003	0.016	0.857
Processed meat	0.025	0.016	0.131	0.150	0.016	< 0.001	-0.006	0.015	0.672
Oily fish	-0.008	0.016	0.617	0.148	0.016	< 0.001	-0.018	0.016	0.252
Non-oily fish	0.003	0.016	0.859	0.148	0.016	< 0.001	0.023	0.016	0.144

CI confidence interval, *GRS* genetic risk score, *MAFLD* metabolic-associated fatty liver disease

Cox proportional hazard regression models for MAFLD were performed using standardized values of meat intake and GRS

[a]β coefficients were adjusted for age, sex, ethnicity, centers, BMI, education, Household income, Townsend deprivation index, smoking, alcohol consumption, physical activity, energy, Alternate Mediterranean Diet score (total score minus the meat component), and other remaining meats

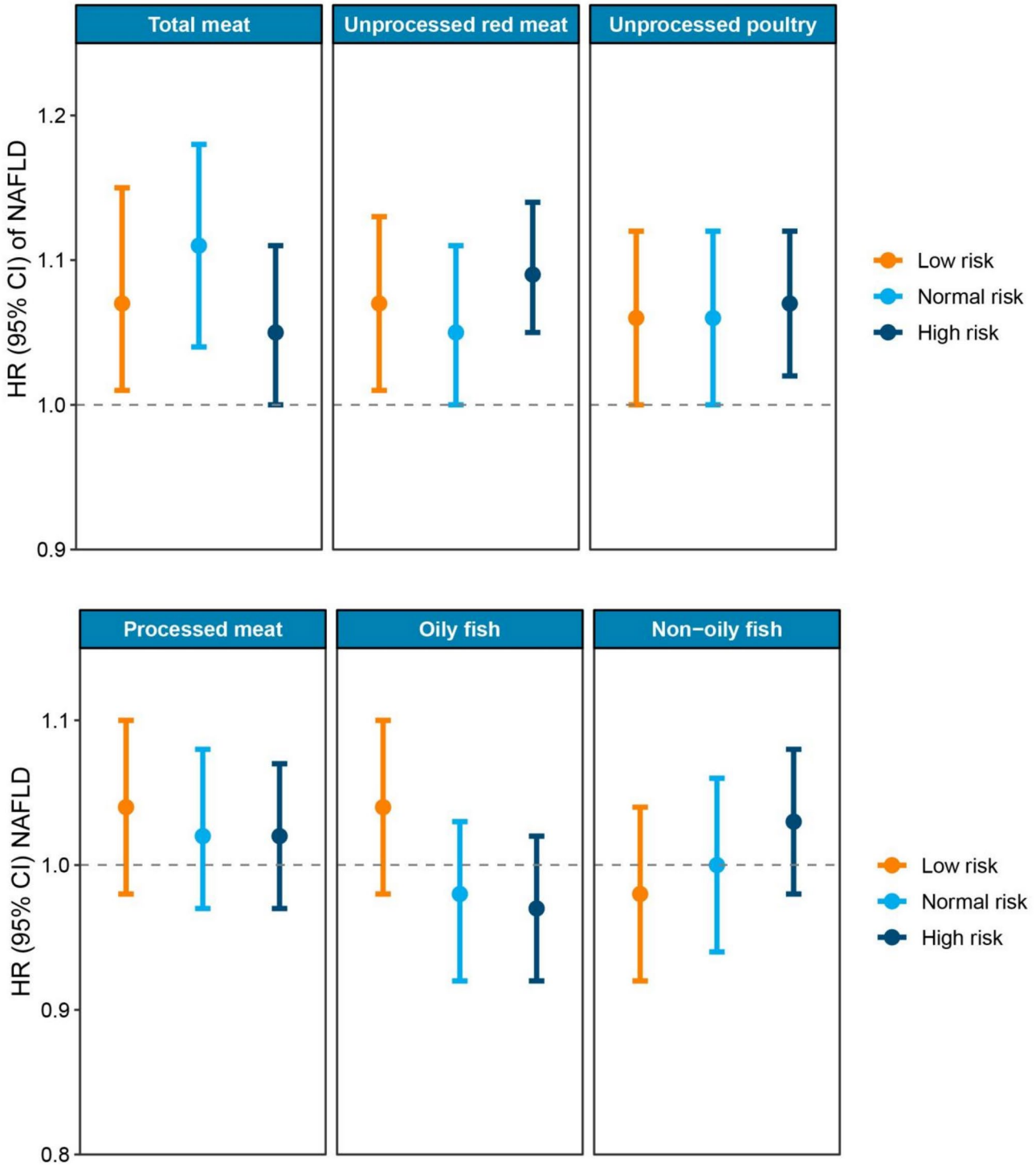

Fig. 2 Hazard ratios for MAFLD for 1 standard deviation increment in meat intake across genetic risk categories. The multivariable model was adjusted for age and sex, ethnicity (White, Asian, Black, mixed, or other ethnic group), centers (22 categories), BMI (in kg/m2; <18.5, 18.5 to 25, 25 to 30, 30 to 35, ≥ 35, or missing), education (college or university degree, vocational qualifications, optional national exams at ages 17–18 years, national exams at age 16 years, others, or missing), Townsend deprivation index (quartiles), household income (<£18,000, £18,000-£30,999, £31,000-£51,999, £52,000-£100,000, >£100,000, or missing), smoking (never, former, current, or missing), alcohol consumption (never or special occasions only, 1 to 3 times/month, 1 or 2 times/week, 3 or 4 times/week, or daily/almost daily), physical activity (in MET-h/wk; quartiles), other remaining meats (unprocessed red meat, processed meat, unprocessed poultry, oily fish and non-oily fish), total energy intake, and Alternate Mediterranean Diet score (total score minus the meat component)

periods to capture long-term effects [33]. However, our large-scale study ($n = 487,875$) with an extended follow-up duration (12.1 years) strongly supports a positive link between high red meat intake and severe MAFLD. Unprocessed red meat is rich in saturated fatty acids (SFAs), which have been shown to increase liver lipid storage, affecting energy metabolism and insulin resistance [34]. These changes potentially promote MAFLD development through the regulation of liver gene expression and signaling. High SFA levels initiate the unfolded protein response by saturating the endoplasmic reticulum (ER) membrane, leading to ER stress and elevated levels of lysophosphatidylcholine (LPC) [35]. Mitochondrial dysfunction also plays a crucial role in the effects of high SFA levels on MAFLD [35]. Additionally, inflammation, oxidative stress, ER stress, and increased LPC levels induced by high SFAs can activate the c-Jun N-terminal kinase (JNK) stress pathway, which promotes hepatocyte apoptosis—a key factor in the development of NASH [36].

Previous studies have shown a significant association between high processed meat intake and an increased risk of severe MAFLD [12–14, 33], which aligns with our findings. However, some research has questioned the strength of this relationship [37], possibly due to differences in sample characteristics and assessment methods. Processed meats are high in SFAs and typically contain elevated levels of sodium (up to 400% more than unprocessed meats) and additives such as nitrites, which have been linked to insulin resistance and oxidative stress, contributing to MAFLD development [38, 39]. High intake of processed meats is also associated with hepatic accumulation of advanced glycation end products (AGEs), which are closely related to the progression of NASH through activation of the TGF-β signaling pathway, a critical factor in liver fibrosis [40].

The relationship between fish consumption and MAFLD has also been contentious [16–18]. Our study revealed that oily fish, but not non-oily fish, was associated with a lower risk of severe MAFLD. Consistent with our findings, a recent South Korean cohort study reported that oily fish and its fatty acids were protective against MAFLD, particularly in women [16]. Similarly, the Guangzhou Biobank Cohort Study found an inverse association between fatty fish consumption and MAFLD [15]. Oily fish is a significant source of n-3 polyunsaturated fatty acids (PUFA) [41], which have been shown to inhibit the activity of sterol regulatory element-binding protein-1c (SREBP-1c) and reduce the cellular abundance of Max-like protein, thereby suppressing fatty acid synthesis and regulating enzymes such as acetyl-CoA carboxylase and fatty acid synthase involved in fat formation [42, 43]. Additionally, n-3 PUFA can promote insulin receptor activation and IRS-1 tyrosine phosphorylation, leading to the activation of the PI3K-Akt pathway and translocation of glucose transporter 4, which enhances glucose uptake into cells and reduces liver fat accumulation [44]. Furthermore, n-3 PUFA acts as a ligand for peroxisome proliferator-activated receptor-α, activating ACOX and medium-chain acyl-CoA dehydrogenase, thus promoting fatty acid β-oxidation [45]. Due to its antioxidative and anti-inflammatory properties, n-3 PUFA shows promise in treating metabolic syndrome, though its effects on oxidative stress have shown variable results [46–48]. Overall, n-3 PUFA appears to play a protective role in the progression of severe MAFLD, supporting recommendations for oily fish consumption to help prevent MAFLD.

Limited data are available on the relationship between poultry consumption and MAFLD. A positive association between poultry intake and MAFLD was reported in a nested case-control analysis of 2,974 MAFLD cases and 29,474 matched controls [22]. However, this association was not observed in the Guangzhou Biobank Cohort Study, which included 1,862 participants aged 50 years or older [15]. Our finding of a positive link between unprocessed poultry consumption and severe MAFLD should be interpreted with caution, as the highest category of consumption (≥ 5 times/week) did not show a statistically significant hazard ratio (HR: 1.21; 95% CI: 0.98–1.49) compared with non-consumers. Additional studies are needed to validate our results.

MAFLD is thought to develop from complex interactions between genetic and lifestyle factors, including diet [24]. However, we did not observe significant interactions between different types of meat consumption and the MAFLD GRS, suggesting that the detrimental effects of red and processed meat and the protective effects of oily fish on MAFLD risk are consistent across varying levels of genetic risk. These findings indicate that dietary guidelines recommending reduced consumption of red and processed meats, along with increased oily fish intake, may be beneficial for the general population regardless of genetic predisposition to MAFLD. Our subgroup analyses further indicated that the associations between red or processed meat intake and MAFLD risk were stronger among younger participants and those without a history of diabetes or hypertension, suggesting that healthier individuals might be more susceptible to the harmful effects of red or processed meat. Excluding individuals with known liver disease at baseline may have disproportionately removed older individuals and those with metabolic conditions, resulting in relatively lower risk in healthier subgroups. However, further mechanistic research is needed to clarify this observation.

The strengths of our study include its large sample size, long duration of follow-up, and the assessment of gene-diet interactions. However, several limitations should be

considered. First, MAFLD diagnosis was based on hospital admission and mortality records, primarily capturing advanced or severe cases, which may have excluded milder instances of the disease. Second, although the FFQ used to assess meat intake was validated, self-reported dietary data are subject to measurement errors. We incorporated 24-hour dietary recall data as a supplementary analysis, which allows for a more precise estimation of meat intake based on food weight. Our findings from 24-hour dietary recall data remained largely consistent with the primary results, although reduced sample size limited statistical power for certain food groups, such as fish. Future studies should integrate comprehensive dietary assessments, including quantitative intake measurements, to corroborate our findings. Third, meat consumption was measured only at baseline, so any dietary changes over time were not captured, which may have led to an underestimation of associations. Fourth, including fish in the "meat" food group presents challenges in interpreting its overall association with MAFLD risk, as meat and fish have divergent health effects. This classification may obscure the distinct roles of different protein sources, with processed and red meats generally increasing risk, while fish consumption tends to offer protective effects. Fifth, despite adjusting for a wide range of covariates, the possibility of unmeasured or residual confounding cannot be completely ruled out. Sixth, our study population consisted only of European men and women, limiting the generalizability of the findings to other ethnic groups. Finally, given the observational design of this study, causal relationships cannot be established.

Conclusions

In conclusion, our study found that higher consumption of total meat, processed meat, and unprocessed red meat was associated with an increased risk of severe MAFLD, while oily fish consumption was associated with a reduced risk. These associations were independent of genetic risk for MAFLD. Our findings provide strong evidence supporting the recommendation to reduce red and processed meat consumption and increase oily fish intake for the primary prevention of MAFLD, regardless of individual genetic risk.

Abbreviations

MAFLD	metabolic-associated fatty liver disease
GRS	Genetic risk scores
HR	hazard ratios
FFQ	food frequency questionnaire
AMED	Alternate Mediterranean Diet
MET	metabolic equivalent of task
SNPs	single nucleotide polymorphisms
NASH	non-alcoholic steatohepatitis
CI	confidence intervals
ER	endoplasmic reticulum

Supplementary Information

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Supplementary Material 1

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Author contributions

PZ and YF conceptualized the study, PZ handled the data curation, JW, JM, and XW compiled the data and performed statistical analyses with supervisory input from PZ and YF All authors contributed to the finalization of statistical models and interpretation of findings, JW and JM wrote the first draft of the manuscript, and XW and PZ critically reviewed and edited the manuscript. All authors read and approved the final manuscript, and accept responsibility for the decision to submit for publication.

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Data availability

The UK Biobank data are available from the UK Biobank on request (www.ukbiobank.ac.uk).

Declarations

Ethics approval and consent to participate

The UK Biobank study was conducted according to the guidelines of the Declaration of Helsinki and approved by the North West Multicentre Research Ethics Committee (REC reference: 21/NW/0157). Informed consent was obtained from all subjects involved in the study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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References

1. Powell EE, Wong VW, Rinella M. Non-alcoholic fatty liver disease. Lancet. 2021;397(10290):2212–24.
2. Devarbhavi H, Asrani SK, Arab JP, Nartey YA, Pose E, Kamath PS. Global burden of liver disease: 2023 update. J Hepatol. 2023;79(2):516–37.

3. Younossi Z, Anstee QM, Marietti M, Hardy T, Henry L, Eslam M, George J, Bugianesi E. Global burden of NAFLD and NASH: trends, predictions, risk factors and prevention. Nat Rev Gastroenterol Hepatol. 2018;15(1):11–20.
4. Younossi ZM. Non-alcoholic fatty liver disease - A global public health perspective. J Hepatol. 2019;70(3):531–44.
5. European Association for the Study of the Liver (EASL). European association for the study of diabetes (EASD); European association for the study of obesity (EASO). EASL-EASD-EASO clinical practice guidelines for the management of non-alcoholic fatty liver disease. J Hepatol. 2016;64(6):1388–402.
6. Clemente-Suárez VJ, Beltrán-Velasco AI, Redondo-Flórez L, Martín-Rodríguez A, Tornero-Aguilera JF. Global impacts of Western diet and its effects on metabolism and health: A narrative review. Nutrients 2023, 15(12).
7. Semmler G, Datz C, Reiberger T, Trauner M. Diet and exercise in NAFLD/NASH: beyond the Obvious. Liver Int. 2021;41(10):2249–68.
8. Berná G, Romero-Gomez M. The role of nutrition in non-alcoholic fatty liver disease: pathophysiology and management. Liver Int. 2020;40(Suppl 1):102–8.
9. Anania C, Perla FM, Olivero F, Pacifico L, Chiesa C. Mediterranean diet and nonalcoholic fatty liver disease. World J Gastroenterol. 2018;24(19):2083–94.
10. Younossi ZM, Zelber-Sagi S, Henry L, Gerber LH. Lifestyle interventions in nonalcoholic fatty liver disease. Nat Rev Gastroenterol Hepatol. 2023;20(11):708–22.
11. Zelber-Sagi S, Nitzan-Kaluski D, Goldsmith R, Webb M, Blendis L, Halpern Z, Oren R. Long term nutritional intake and the risk for non-alcoholic fatty liver disease (NAFLD): a population based study. J Hepatol. 2007;47(5):711–7.
12. Zelber-Sagi S, Ivancovsky-Wajcman D, Fliss Isakov N, Webb M, Orenstein D, Shibolet O, Kariv R. High red and processed meat consumption is associated with non-alcoholic fatty liver disease and insulin resistance. J Hepatol. 2018;68(6):1239–46.
13. Kim MN, Lo CH, Corey KE, Luo X, Long L, Zhang X, Chan AT, Simon TG. Red meat consumption, obesity, and the risk of nonalcoholic fatty liver disease among women: evidence from mediation analysis. Clin Nutr. 2022;41(2):356–64.
14. Charatcharoenwitthaya P, Tansakul E, Chaiyasoot K, Bandidniyamanon W, Charatcharoenwitthaya N. Dietary composition and its association with newly diagnosed nonalcoholic fatty liver disease and insulin resistance. Nutrients 2021, 13(12).
15. Wang RZ, Zhang WS, Jiang CQ, Zhu F, Jin YL, Xu L. Association of fish and meat consumption with non-alcoholic fatty liver disease: Guangzhou biobank cohort study. BMC Public Health. 2023;23(1):2433.
16. Tan LJ, Shin S. Effects of oily fish and its fatty acid intake on non-alcoholic fatty liver disease development among South Korean adults. Front Nutr. 2022;9:876909.
17. He K, Guo LL, Tang H, Peng X, Li J, Feng S, Bie C, Chen W, Li Y, Wang M, et al. A freshwater Fish-Based diet alleviates liver steatosis by modulating gut microbiota and metabolites: A clinical randomized controlled trial in Chinese participants with nonalcoholic fatty liver disease. Am J Gastroenterol. 2022;117(10):1621–31.
18. Yabe Y, Chihara K, Oshida N, Kamimaki T, Hasegawa N, Isobe T, Shoda J. Survey of dietary habits and physical activity in Japanese patients with Non-Obese Non-Alcoholic fatty liver disease. Nutrients 2023, 15(12).
19. Katsagoni CN, Georgoulis M, Papatheodoridis GV, Fragopoulou E, Ioannidou P, Papageorgiou M, Alexopoulou A, Papadopoulos N, Deutsch M, Kontogianni MD. Associations between lifestyle characteristics and the presence of non-alcoholic fatty liver disease: A Case-Control study. Metab Syndr Relat Disord. 2017;15(2):72–9.
20. Chan R, Wong VW, Chu WC, Wong GL, Li LS, Leung J, Chim AM, Yeung DK, Sea MM, Woo J, et al. Diet-Quality scores and prevalence of nonalcoholic fatty liver disease: A population study using Proton-Magnetic resonance spectroscopy. PLoS ONE. 2015;10(9):e0139310.
21. Shi L, Liu ZW, Li Y, Gong C, Zhang H, Song LJ, Huang CY, Li M. The prevalence of nonalcoholic fatty liver disease and its association with lifestyle/dietary habits among university faculty and staff in Chengdu. Biomed Environ Sci. 2012;25(4):383–91.
22. Noureddin M, Zelber-Sagi S, Wilkens LR, Porcel J, Boushey CJ, Le Marchand L, Rosen HR, Setiawan VW. Diet associations with nonalcoholic fatty liver disease in an ethnically diverse population: the multiethnic cohort. Hepatology. 2020;71(6):1940–52.
23. Trépo E, Valenti L. Update on NAFLD genetics: from new variants to the clinic. J Hepatol. 2020;72(6):1196–209.
24. Liu Z, Huang H, Ruan J, Wang Z, Xu C. The sulfur microbial diet and risk of nonalcoholic fatty liver disease: a prospective gene-diet study from the UK biobank. Am J Clin Nutr. 2024;119(2):417–24.
25. Anstee QM, Seth D, Day CP. Genetic factors that affect risk of alcoholic and nonalcoholic fatty liver disease. Gastroenterology. 2016;150(8):1728–e17441727.
26. Sudlow C, Gallacher J, Allen N, Beral V, Burton P, Danesh J, Downey P, Elliott P, Green J, Landray M, et al. UK biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old age. PLoS Med. 2015;12(3):e1001779.
27. Fung TT, McCullough ML, Newby PK, Manson JE, Meigs JB, Rifai N, Willett WC, Hu FB. Diet-quality scores and plasma concentrations of markers of inflammation and endothelial dysfunction. Am J Clin Nutr. 2005;82(1):163–73.
28. Zhuang P, Liu X, Li Y, Wan X, Wu Y, Wu F, Zhang Y, Jiao J. Effect of diet quality and genetic predisposition on hemoglobin A(1c) and type 2 diabetes risk: Gene-Diet interaction analysis of 357,419 individuals. Diabetes Care. 2021;44(11):2470–9.
29. Townsend P, Deprivation. J Social Policy. 1987;16(2):125–46.
30. World Health Organization G. WHO guidelines approved by the guidelines review committee. *Global recommendations on physical activity for health Geneva, Switzerland: World Health Organization* 2010.
31. Huang T, Qi Q, Zheng Y, Ley SH, Manson JE, Hu FB, Qi L. Genetic predisposition to central obesity and risk of type 2 diabetes: two independent cohort studies. Diabetes Care. 2015;38(7):1306–11.
32. Petermann-Rocha F, Gray SR, Forrest E, Welsh P, Sattar N, Celis-Morales C, Ho FK, Pell JP. Associations of muscle mass and grip strength with severe NAFLD: A prospective study of 333,295 UK biobank participants. J Hepatol. 2022;76(5):1021–9.
33. Zhou Q, Hu H, Hu L, Liu S, Chen J, Tong S. Association between processed and unprocessed red meat consumption and risk of nonalcoholic fatty liver disease: A systematic review and dose-response meta-analysis. J Glob Health. 2024;14:04060.
34. Hernández E, Kahl S, Seelig A, Begovatz P, Irmler M, Kupriyanova Y, Nowotny B, Nowotny P, Herder C, Barosa C, et al. Acute dietary fat intake initiates alterations in energy metabolism and insulin resistance. J Clin Invest. 2017;127(2):695–708.
35. Leamy AK, Egnatchik RA, Young JD. Molecular mechanisms and the role of saturated fatty acids in the progression of non-alcoholic fatty liver disease. Prog Lipid Res. 2013;52(1):165–74.
36. Singh R, Wang Y, Xiang Y, Tanaka KE, Gaarde WA, Czaja MJ. Differential effects of JNK1 and JNK2 Inhibition on murine steatohepatitis and insulin resistance. Hepatology. 2009;49(1):87–96.
37. Peng H, Xie X, Pan X, Zheng J, Zeng Y, Cai X, Hu Z, Peng XE. Association of meat consumption with NAFLD risk and liver-related biochemical indexes in older Chinese: a cross-sectional study. BMC Gastroenterol. 2021;21(1):221.
38. Fahed G, Aoun L, Bou Zerdan M, Allam S, Bou Zerdan M, Bouferraa Y, Assi HI. Metabolic syndrome: updates on pathophysiology and management in 2021. Int J Mol Sci 2022, 23(2).
39. Shoelson SE, Lee J, Goldfine AB. Inflammation and insulin resistance. J Clin Invest. 2006;116(7):1793–801.
40. Hyogo H, Yamagishi S, Iwamoto K, Arihiro K, Takeuchi M, Sato T, Ochi H, Nonaka M, Nabeshima Y, Inoue M, et al. Elevated levels of serum advanced glycation end products in patients with non-alcoholic steatohepatitis. J Gastroenterol Hepatol. 2007;22(7):1112–9.
41. Bonsembiante L, Targher G, Maffeis C. Non-alcoholic fatty liver disease in obese children and adolescents: a role for nutrition? Eur J Clin Nutr. 2022;76(1):28–39.
42. Scorletti E, Byrne CD. Omega-3 fatty acids and non-alcoholic fatty liver disease: evidence of efficacy and mechanism of action. Mol Aspects Med. 2018;64:135–46.
43. Moslehi A, Hamidi-Zad Z. Role of SREBPs in liver diseases: A Mini-review. J Clin Transl Hepatol. 2018;6(3):332–8.
44. Nardi F, Lipina C, Magill D, Hage Hassan R, Hajduch E, Gray A, Hundal HS. Enhanced insulin sensitivity associated with provision of mono and polyunsaturated fatty acids in skeletal muscle cells involves counter modulation of PP2A. PLoS ONE. 2014;9(3):e92255.
45. Pettinelli P, Videla LA. Up-regulation of PPAR-gamma mRNA expression in the liver of obese patients: an additional reinforcing lipogenic mechanism to SREBP-1c induction. J Clin Endocrinol Metab. 2011;96(5):1424–30.
46. González-Périz A, Planagumà A, Gronert K, Miquel R, López-Parra M, Titos E, Horrillo R, Ferré N, Deulofeu R, Arroyo V, et al. Docosahexaenoic acid (DHA)

blunts liver injury by conversion to protective lipid mediators: protectin D1 and 17S-hydroxy-DHA. Faseb J. 2006;20(14):2537–9.
47. Neuhofer A, Zeyda M, Mascher D, Itariu BK, Murano I, Leitner L, Hochbrugger EE, Fraisl P, Cinti S, Serhan CN, et al. Impaired local production of proresolving lipid mediators in obesity and 17-HDHA as a potential treatment for obesity-associated inflammation. Diabetes. 2013;62(6):1945–56.
48. Yang J, Fernández-Galilea M, Martínez-Fernández L, González-Muniesa P, Pérez-Chávez A, Martínez JA, Moreno-Aliaga MJ. Oxidative stress and Non-Alcoholic fatty liver disease: effects of Omega-3 fatty acid supplementation. Nutrients 2019, 11(4).

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