

Dietary and physical activity risk and protective factors for lean non-alcoholic fatty liver disease: A scoping review

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Abstract

Non-Alcoholic Fatty Liver Disease (NAFLD) is one of the most common causes of chronic liver disease globally and describes a spectrum of conditions ranging from simple hepatic steatosis to liver cirrhosis and/or failure. Although it is more prevalent in populations with metabolic risk factors including obesity, insulin resistance, dyslipidemia, and type 2 diabetes, it can also occur in lean populations who may or may not present with symptoms of NAFLD. Consequently, lean populations with NAFLD can be overlooked in both clinical and research settings. Despite the associations between diet and physical activity and the prevention of many chronic diseases, primary research exploring the association between diet and physical activity and NAFLD risk in lean populations is lacking. The purpose of this scoping review was to describe the available research on dietary and physical activity risk and protective factors in lean NAFLD, define key terms related to this condition, and identify knowledge gaps to inform future research.

A literature search was conducted between March 2021 and August 2023 in PubMed, Global Health, ProQuest Nursing and Allied Health, Web of Science, and Scopus. Sixty-four articles were included in the review. The predominant study designs were cross-sectional and prospective. More than half of the studies were based in Asia. Research topics included the associations between specific diets, food groups, macronutrients, micronutrients, beverages, and varying physical activity characteristics, and lean NAFLD risk.

Very few definitive conclusions could be made about potential dietary or physical activity risk and protective factors for lean NAFLD due to several limitations in the current body of evidence. These limitations included a high risk for bias and lack of ethnic diversity in study populations, as well as significant heterogeneity in results, definitions of key terms, and NAFLD

diagnostic criteria. To address these deficits, future research is needed on topics explored in the current body of evidence, using higher quality study designs that limit the risk of bias, integrate more ethnic diversity in study populations, and implement consistent terminology and NAFLD diagnostic criteria.

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List of Abbreviations

AFLD: Alcoholic Fatty Liver Disease

AMED: Adjusted Mediterranean Diet

ALT: Alanine transaminase

AST: Aspartate transaminase

B-vitamins: Thiamin (vitamin B1), Riboflavin (B2), Niacin (B3), Pantothenic acid (B5),
Pyridoxine (B6), Biotin (B7), Folate (B9), and Cyanocobalamin (B12)

BMI: Body Mass Index

CAD: Coronary Artery Disease

CD: Celiac Disease

CT: Computed Tomography

CVD: Cardiovascular Disease

DASH: Dietary Approaches to Stop Hypertension

DHA: Docosahexaenoic acid

DM: Diabetes

EPA: Eicosapentaenoic acid

FFQ: Food Frequency Questionnaire

FLI: Fatty Liver Index

FLD: Fatty Liver Disease

FPG: Fasting Plasma Glucose

FRUVED + LF: Fruit and Vegetable Diet + Low Fat

FRUVED + LRC: Fruit and Vegetable Diet + Low Refined Carbohydrate

GFD: Gluten Free Diet

GGT: Gamma-glutamyl transferase

GI: Gastrointestinal

GLV: Green Leafy Vegetables

H-MRS: Proton Magnetic Resonance Spectroscopy

HbA1c: Hemoglobin A1c Test

HBV: Hepatitis B Virus

HBP: High Blood Pressure

HCC: Hepatocellular Carcinoma

HCLP: High Carbohydrate Low Protein Diet

HCV: Hepatitis C Virus

HEPA: Health Enhancing Physical Activity

HIV: Human Immunodeficiency Virus

HLD: Hyperlipidemia

HLS: Healthy Living Score

HPLC: High Protein Low Carbohydrate Diet

HOMA-IR: Homeostatic Model Assessment for Insulin Resistance

HRI: Hepatorenal Index

HS: Hepatic Steatosis

HTN: Hypertension

IDF: International Diabetes Federation

IHTG: Intrahepatic Triglycerides

IPAQ: International Physical Activity Questionnaire

IR: Insulin Resistant

IS: Insulin Sensitive

K: Potassium

MAFLD: Metabolic Dysfunction Associated Fatty Liver Disease

MDS: Mediterranean Diet Score

MET: Metabolic Equivalent of Task

MetS: Metabolic Syndrome

MRI: Magnetic Resonance Imaging

MUFA: Monounsaturated Fatty Acid

Na: Sodium

Na: K ratio: Sodium to Potassium ratio

NAFLD: Non-Alcoholic Fatty Liver Disease

NASH: Non-Alcoholic Steatohepatitis

NCEP: National Cholesterol Education Program

PA: Physical Activity

PAI: Physical Activity Index

PAL: Physical Activity Level

PBC: Primary biliary cholangitis

PRISMA-ScR: Preferred Reporting Items for Systematic reviews and Meta-Analyses Extension
for Scoping Reviews

PUFA: Polyunsaturated Fatty Acid

PUFA: SFA ratio: Polyunsaturated Fatty Acid to Saturated Fatty Acid ratio

SFA: Saturated Fatty Acid

T2DM: Type 2 Diabetes

TE: Transient Elastography

TG: Triglycerides

US: Ultrasound

WC: Waist Circumference

WHR: Waist-to-Hip Ratio

Chapter 1 - Introduction

Nonalcoholic Fatty Liver disease (NAFLD) is one of the most common causes of chronic liver disease globally and is a condition characterized by excessive hepatic steatosis without the presence of secondary causes of liver disease¹⁻⁴. These secondary causes include viral hepatitis, hypothyroidism, and hereditary liver diseases. Other causes include excessive alcohol intake, which is most often defined as > 30 g ethanol/day for males and > 20 g ethanol/day for females though the definition can vary significantly³⁻⁶. The term NAFLD describes a spectrum of conditions ranging from hepatic steatosis (HS) without liver injury, to more severe health conditions including hepatic inflammation (NASH), hepatocellular carcinoma, and/or liver failure potentially requiring transplantation. NAFLD is commonly associated with metabolic irregularities including insulin resistance (IR), metabolic syndrome (MetS), dyslipidemia, and type 2 diabetes mellitus (T2DM)^{2,4,5}. NAFLD can share overlapping characteristics and pathology with Alcoholic Fatty Liver Disease (AFLD) and may even occur concurrently with AFLD^{5,7}. In fact, more recent literature suggests that NAFLD should be referred to as Metabolic Dysfunction Associated Fatty Liver Disease (MAFLD) to better distinguish its pathologies from AFLD, though this term has not been consistently used in literature^{4,5}.

Although NAFLD is most commonly found in those with overweight or obesity, it has also been found in some individuals who are classified as lean. These individuals may or may not present with symptoms of metabolic irregularities that are as severe as those that occur in patients with obese NAFLD¹. The exact definition of lean varies in the literature, as anthropometric parameters including body mass index (BMI), waist circumference (WC), and waist-to-hip ratio (WHR) can be classified differently based on ethnicity and/or how researchers interpret and apply published guidelines from professional organizations. In the past decade, lean

Asian populations have been defined as having BMIs $< 23\text{--}24 \text{ kg/m}^2$ (depending on the Asian subgroup) and lean non-Asian populations have been defined as BMIs $< 25 \text{ kg/m}^2$ ^{1,8–11}. The term is often used interchangeably with non-obese despite differences in definition. Most often, the term non-obese refers to those classified as underweight, normal weight, or overweight, and defined as BMIs $< 25\text{--}28 \text{ kg/m}^2$ for Asian populations (depending on the Asian subgroup) and BMIs $< 30 \text{ kg/m}^2$ for non-Asian populations. The implementation of these definitions varies in research and clinical practice^{1,12–14}. Ethnicity-specific anthropometric measures are not always utilized and terms such as lean and non-obese are used synonymously^{1,13,15}. The lack of consensus on how to classify weight status illustrates the challenges of understanding a state of leanness using population-level BMI data, especially without a valid individual level body composition measure^{1,8,13,14}. For the purposes of this scoping review, we defined lean as individuals who are not overweight or obese and with a BMI $< 25 \text{ kg/m}^2$ in an effort to capture the heterogeneity in anthropometric thresholds used in the literature, and to fully explore the available research on this topic.

Globally, the prevalence of lean NAFLD varies depending on the population being studied, anthropometric parameters used to categorize weight status, NAFLD diagnostic methods, and whether authors distinguish between lean and non-obese NAFLD. Overall, epidemiological studies indicate that 15% of Asian populations and 9% of Western populations have lean NAFLD^{1,6,11,16,17}. Among all NAFLD cases globally, it has been reported that 31% of patients in Asia and 15.5% of patients in Western countries have lean NAFLD⁶. Prevalence rates in individual Asian countries including China, Korea, or Iran range from 4.3–5.5%, while rates in Europe and the United States of America are 2.2% and 7% respectively^{17,18}. Although prevalence rates of lean NAFLD may appear to be relatively low, it has been noted that these

rates have steadily increased in the past twenty years and they may be considerably underestimated due to the heterogeneity of definitions and diagnostic criteria applied in research and clinical settings¹⁹.

The potential risk for development of NAFLD in lean patients may be overlooked in clinical settings due to a lack of obvious risk factors including elevated BMI and metabolic abnormalities such as significant hyperglycemia^{3,4,15,17,20,21}. Even if fatty liver is detected, it typically appears to be a less severe phenotype compared to obese NAFLD, and may not be as closely monitored¹. However, lean NAFLD patients can still experience HS, lobular inflammation, fibrosis, and increased risk for MetS, T2DM, and cardiovascular diseases. In fact, research indicates that those with lean NAFLD had higher prevalence of metabolic, cardiovascular, and cancer comorbidities compared to those with obese NAFLD or no NAFLD^{1,11,15}. Patients with lean NAFLD were also found to have higher prevalence of advanced liver fibrosis and similar prevalence of T2DM compared to those with obese NAFLD. Furthermore, it was found that advanced fibrosis and T2DM contributed to higher all-cause mortality rates in those with lean NAFLD compared to those with obese NAFLD¹¹. The combination of these health risks, potential effects on quality of life, and financial losses related to healthcare costs, clearly indicate that lean NAFLD should not be overlooked^{2,5}.

Despite the aforementioned concerns and potential health risks, research examining risk factors, pathology, and appropriate treatments for lean NAFLD is limited. Given the significant association between obesity and NAFLD risk, treatment recommendations are often focused on dietary and/or physical activity interventions^{1,4,7,22}. In addition, previous research has also shown weight loss effectively reduces hepatic fat content in populations with obesity^{4,15}. However, it is unclear whether dietary and/or physical activity interventions can provide the same benefits for

lean individuals who do not have excess body weight⁴. Historically, the guidelines for NAFLD management published by professional governing bodies have provided minimal discussion of lean NAFLD with few specific guidelines for this population³. However, since 2020, professional organizations have published practice guidelines for treating this patient population. Recommendations include following a Mediterranean diet, exercise, limiting saturated fats and refined carbohydrates, and weight loss of at least 3–5% of body weight^{4,5,15}. Many of the recommendations are based on studies utilizing either obese NAFLD populations or smaller, short-term interventional studies with non-obese (not necessarily lean) participants. The guidelines also do not explore other avenues of nutrition intervention, such as modifying specific nutrient intakes, and they disagree regarding the extent of recommended weight loss in the lean NAFLD population^{4,5,15}. Some guidelines even acknowledge that weight loss and/or hypocaloric diet recommendations may not apply to this population because so little is known about lean NAFLD⁴. In addition to the lack of overall clinical practice guidelines for treating this specific population, there are currently no systematic reviews and meta-analyses that have analyzed nutrition interventions as well as dietary and/or physical activity risk factors for lean NAFLD. Therefore, we determined that a scoping review was needed as a first step toward addressing these knowledge gaps and guiding future research on lean NAFLD. The primary objective of this scoping review was to provide an overview of the available published research on dietary and/or physical activity risk and protective factors for NAFLD in lean adults. The other aim of this scoping review was to identify extant research gaps, inform future clinical interventions, and elucidate current definitions and terminology relevant to how weight status and NAFLD are defined in lean populations.

Chapter 2 - Methods

2.1 Search Strategy

A scoping review was selected to explore the topic of dietary and physical activity risk and protective factors in lean NAFLD due to an initial literature search indicating a significant deficit in research on the topic. Reporting of the review process adhered to the Preferred Reporting Items for Systematic reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) Checklist²³. A research librarian was consulted to determine search strategies including selection of databases, MeSH terms, and keywords. A literature search was conducted between March 2021 and August 2023 in PubMed, Global Health, ProQuest Nursing and Allied Health, Web of Science, and Scopus. MeSH terms used in the search were “diet”, “diet, healthy”, “diet records”, “nutrition assessment”, “life style”, “healthy lifestyle”, “risk factors”, “epidemiology”, “non-alcoholic fatty liver disease”, “fatty liver”, “adult”, “female”, “male”, “humans”, “body mass index”, “waist circumference”, and “thinness/complications”. Additionally, several keywords were included in searches because it was noted after the initial literature search, that NAFLD has several spelling variations and can be referred to using a variety of terms (i.e., non-alcoholic fatty liver disease, nonalcoholic fatty liver disease, non alcoholic fatty liver disease, hepatic steatosis, or fatty liver disease) and there are no current MeSH terms available to search for “non-obese” or “lean” participants with NAFLD. Keywords utilized in the search included “NASH”, “NAFLD”, “non-alcoholic steatohepatitis”, “hepatic steatosis”, “lean”, “nonobese”, “non-obese”, “non-overweight”, “normal weight”, or “healthy weight”. Search strategies were adjusted for each database (see Table A.1 in Appendix A for keywords searches for each database). In addition to database searches, records were also retrieved using forward and backward tracing with article citations.

2.2 Eligibility Criteria

The inclusion and exclusion criteria were selected with the goal of being broad enough to capture the heterogeneity in anthropometric thresholds to categorize body weight, excessive alcohol consumption, and overall NAFLD definitions without including irrelevant topics. Inclusion criteria for records identified in the search required all of the following: (1) adult participants ≥ 18 years old, (2) at least one group of participants with mean or median BMIs < 25 kg/m² and/or WCs < 102 cm (males) or < 88 cm (females) who were diagnosed with NAFLD, MAFLD, NASH, or determined to have fatty liver using liver biopsy, MRI, ultrasound, fatty liver scoring equations, and/or liver function tests, and (3) objective of the study was to evaluate dietary or physical activity risk and/or protective factors for NAFLD or fatty liver. Articles were excluded for the following reasons (1) if a portion of participants met anthropometric parameters to be classified as lean, but results on dietary and/or physical activity risk factors were not stratified to distinguish this group from overweight and obese participants, (2) anthropometric data were not provided, (3) study examined topics other than dietary and/or physical activity risk factors related to fatty liver or NAFLD, (4) indirect measures of dietary intake used including serum or plasma levels of vitamins and minerals, (5) sample exclusively included participants with other known causes of liver disease including AFLD or hepatitis, (6) study was written in a language other than English, (7) article full text was not available, and (8) article was a narrative review, systematic review and meta-analysis, or thesis dissertation. There were no date restrictions during the study selection process.

Included articles were limited to those with adult participants due to concerns that including children and adolescents may present extraneous confounding factors such as hormones and rapid growth patterns seen in pediatric populations. Although the focus of the

scoping review was specifically on NAFLD, it was noted during initial literature searches that several studies explored risk factors for lean NAFLD in terms of the effects of either dietary or physical activity habits on “fatty liver”. Given that fatty liver may appear subsequent to meeting the traditional NAFLD diagnostic criteria, and the fact that lean individuals with NAFLD can experience detrimental effects on liver health with less severe fatty liver as compared to obese populations, these broader inclusion criteria were utilized to fully evaluate contributing risk factors in this population¹. This broader scope could also account for alternative definitions of NAFLD, given that some research considers lean NAFLD to be a metabolic disorder (referred to as MAFLD), and a general lack of consensus on definition of excessive alcohol intake in the scientific community^{5–7,24}.

As previously discussed, BMI < 25 kg/m² was used to best capture the scope of the research given the heterogeneity of anthropometric thresholds used in the literature and the impracticality of applying ethnicity-specific parameters if they are not consistently implemented by researchers. Because BMI lacks accuracy in identifying abdominal adiposity, the screening criteria also included WC^{25,26}. Waist circumference was chosen over WHR because it is considered more practical to measure in research settings and during an initial literature search for the review, WC was found to be more commonly used²⁵. Similar to the challenges seen with identifying appropriate BMI cut-offs to identify lean individuals, there are a variety of WC thresholds used in research²⁶. The most used parameters by international organizations are those established by the National Cholesterol Education Program (NCEP) and International Diabetes Federation (IDF)²⁵. The NCEP categorizes WC of > 102 cm for males and > 88 cm for females as indicating abdominal adiposity while the IDF has more specific guidelines based on ethnicity and risk for obesity and metabolic syndrome ranging from >90–94 cm for males and > 80–90 cm

for females²⁵. The least restrictive WC threshold for lean established by the NCEP was used because it was impractical to apply more specific WC guidelines given the heterogeneity in the medical history of the populations being studied and not always knowing full details about participant ethnicities²⁵.

2.3 Screening for Eligibility

Two independent reviewers examined and selected studies based on inclusion and exclusion criteria. Titles and abstracts were reviewed during an initial search and then full texts were reviewed for those that met eligibility criteria. Disagreements in categorization were discussed until a consensus was reached. Figure 2.1 illustrates the screening and study selection process.

2.4 Data Extraction and Analysis

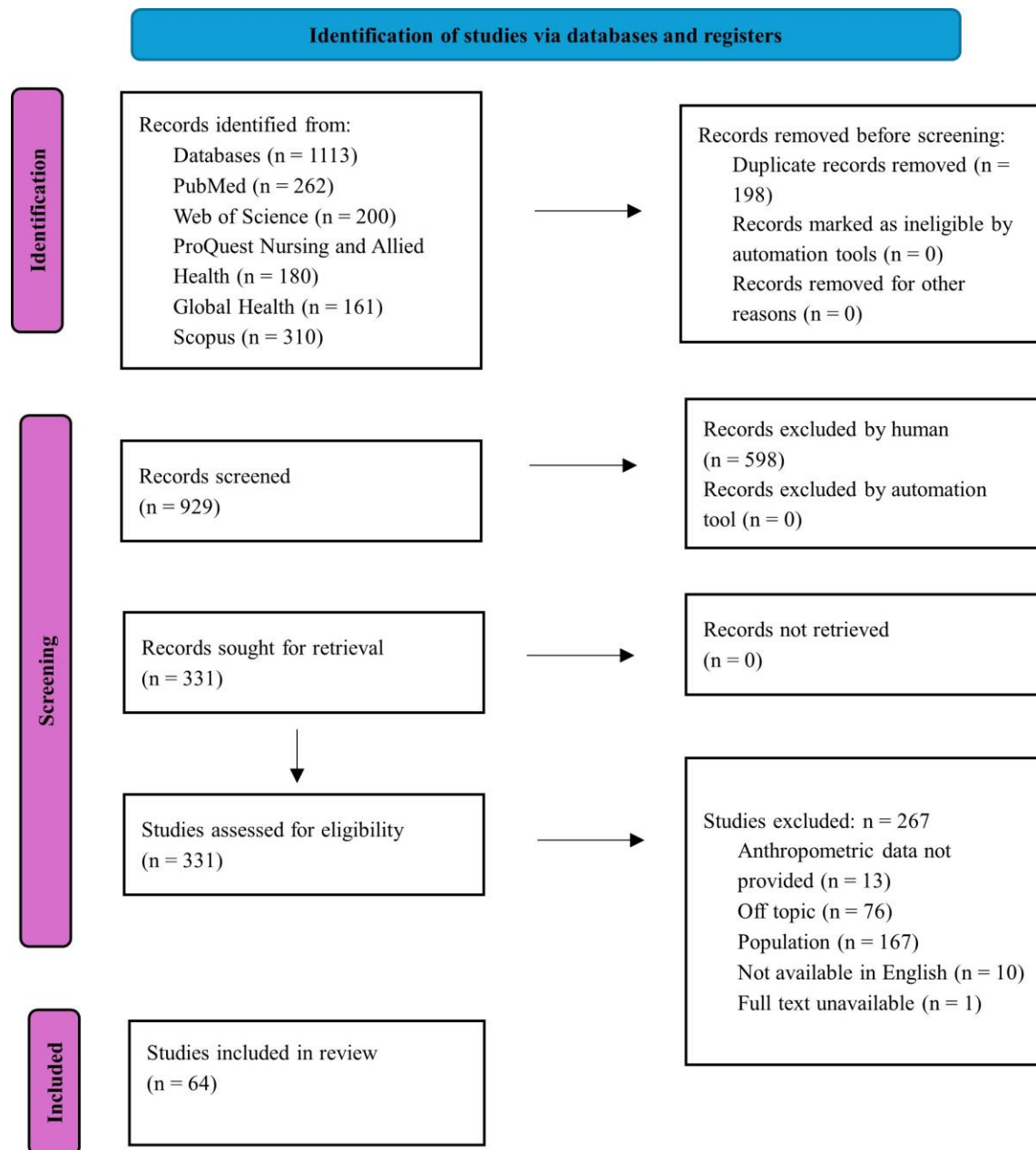
Articles selected for inclusion were reviewed and most relevant data were summarized in an Excel spreadsheet. Details included author, publication date, country of origin, study design, sample size, participant characteristics (sex and age), anthropometric measures and weight status classification per authors, NAFLD diagnostic criteria, and main findings. The main findings were then sorted into four major categories including (1) eating patterns related to lean NAFLD or fatty liver, (2) calorie intake and specific nutrients related to lean NAFLD or fatty liver, (3) beverages choices related to lean NAFLD or fatty liver, and (4) physical activity habits related to lean NAFLD or fatty liver. Tables 3.1 – 3.4 provide a summary of the extracted data.

2.5 Risk of Bias Assessment

Quality appraisal assessments were not utilized in this scoping review due to the significant heterogeneity in study designs and limited use of high-quality designs including randomized control trials and prospective studies. However, all studies that met inclusion criteria

were assessed for limitations including risk of bias based on methodology by one reviewer. If one reviewer was unsure of quality assessment results, a second reviewer was consulted to discuss discrepancies and come to a consensus.

Figure 2.1. PRISMA Flow Diagram



Chapter 3 - Results

3.1 Study Characteristics

The database search generated a total of 1128 records (262 from PubMed, 200 from Web of Science, 180 from ProQuest Nursing and Allied Health, 310 from Scopus, 161 from Global Health, and 15 from other Search Methods). After the removal of duplicates and initial screening of titles and abstracts, the total number of articles was narrowed to 331. Following the review of the full texts of these articles, 64 articles met eligibility criteria and were selected to be included in this scoping review. The primary reason for article exclusion was related to incorrect population characteristics (n = 167). Other reasons for exclusion included off topic (n = 76), anthropometric data was not provided (n = 13), not available in English (n = 10), and full text not available (n = 1).

The year of publication for included articles ranged from 2003 to 2023, though 53 out of the total 64 articles were published in the past 10 years. The countries of origin for the studies included USA^{18,27,28}, Canada²⁹, Mexico³⁰, Brazil³¹, Sweden³², Finland^{33–35}, Germany^{36,37}, Switzerland³⁸, Netherlands³⁹, Italy^{40–44}, South Korea^{10,45–53}, Japan^{9,20,54–68}, China^{69–83}, Iran⁸⁴, India⁸⁵, and Taiwan⁸⁶ (see Figure 3.1). However, 70% of the studies were based in Asia and thus ethnicities residing in South Korea, Japan, and China were predominantly represented in the literature. Ethnicities were not specified in studies based in Europe, Canada, Mexico, and Brazil^{29–39}. Studies conducted in the United States provided vague details on ethnicities, noting participants were either predominantly “White” or approximately 50% “White” or “Black”^{18,27}. However, one study noted that the sample included White, African American, Hispanic, Asian, Other, Appalachian, and Non-Appalachian participants²⁸.

The most common study designs were cross-sectional (59.3%) and prospective (23.4%), with smaller numbers of pre and post intervention (9.4%), retrospective longitudinal (4.7%), and matched case-control studies (3.1%). There were no randomized controlled trials. Figure 3.2 shows the study design distribution. Twenty-seven of the cross-sectional and prospective studies relied on data from ongoing cohort studies, though there was minimal overlap in the cohorts that were studied^{10,18,27,33–35,38,46,48,50,52,53,61,62,65,69,71–73,75–77,80–83,86}. However, seven studies obtained data from an ongoing prospective study in China called Tianjin Chronic Low-grade Systemic Inflammation and Health (TCLSIH) Cohort Study and recruited participants during overlapping dates^{71–73,77–79,82}.

Figure 3.1. Country of Origin Distribution

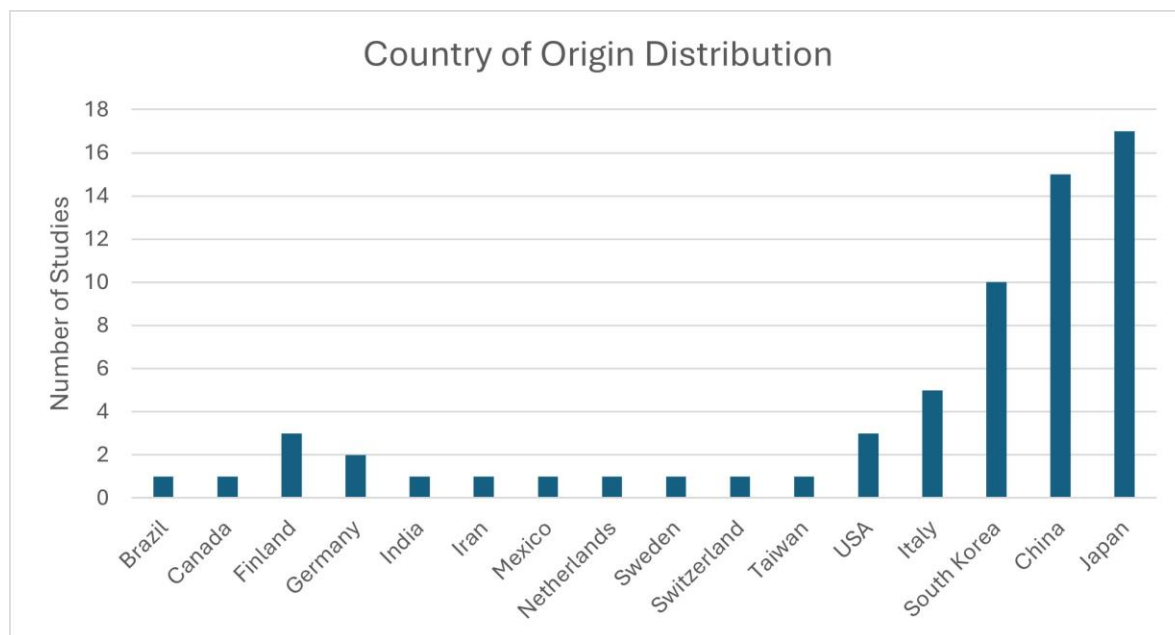
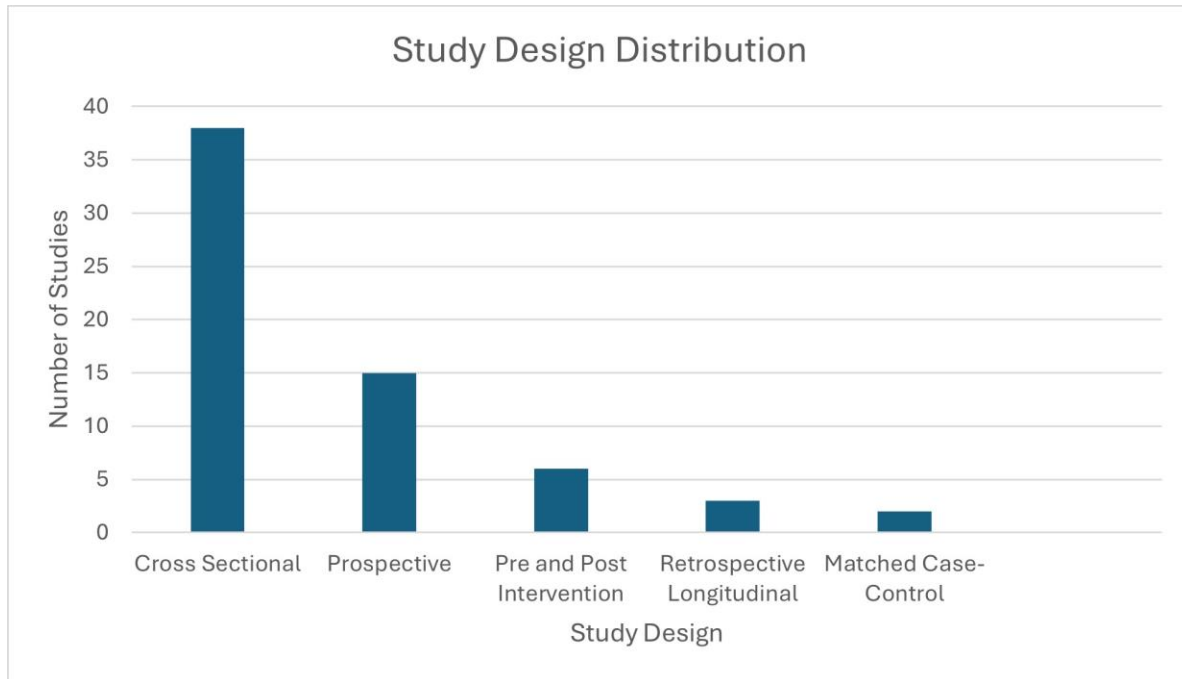


Figure 3.2. Study Design Distribution



Excluding the consistency of the literature largely being focused on Asian populations, there was significant heterogeneity in other characteristics of the studies including sample size, sex distribution, and mean age. The number of participants ranged from as few as 12 participants in an intervention study to over 190,000 participants in a prospective study^{36,52}. Similarly, the demographic characteristics of the sample populations varied. Most studies were characterized by mean ages ranging from early 40's to early 60's, though five studies involved a younger population ranging from age 23 to 26 years old^{28,32,36,37,39}. Additionally, 21 studies used an age restriction in the inclusion criteria and limited participants to “middle age” (approximately 40-75 years old) due to evidence suggesting that NAFLD peaks at this age range^{10,27,29,31,35,36,38,43,48,58–60,63,65,68,69,74–76,81,83}. This increased the overall average age of the population being represented in the studies. For sex distribution, most studies included female and male participants with either

sex being 40-50% of the sample population. However, eight studies involved samples comprised of 100% male^{33,54,55,63,67,83} or 100% female^{27,36}.

Data collection methodology vastly differed across the body of evidence. The most common dietary intake data collection methods included 24-hour dietary recalls^{28,37,50}, food records (ranging from three to seven days in length)^{10,29–32,36,43,44,63,64,66}, unspecified questionnaires^{10,20,33,35,47,55,61,67,69,80,83,85}, and versions of Food Frequency Questionnaires (FFQ) that were tailored to the study population's typical dietary patterns and collected information on habits during a time frame ranging from the past one to twelve months^{9,18,27,34,38,43,46(p201),48,51–53,58–60,62,65,70–79,81,82,84,86}. Data on physical activity was collected using questionnaires similar to International Physical Activity Questionnaire (IPAQ)^{37,46,51–53,77–79,82} or unspecified questionnaires^{9,10,18,20,27,28,33–35,38,39,43,45,48,49,55,58–62,67,69–73,75,76,80,83,85,86}. However, there was inconsistency in the number of details provided on how dietary and physical activity data was collected. Approximately half of the studies did not clarify whether questionnaires were interviewer administered or self-administered, as well as the time frame participants referenced when reporting on usual dietary and/or physical activity habits^{9,18,20,31,33–35,39,40,47,48,50,53–56,58,61–63,65,67,68,71,72,74,75,80,81,83–87}. Additionally, some studies only collected data on specific factors such as alcohol intake, diet, or physical activity rather than evaluating all of these habits in the sample population^{9,10,30–32,36,40–42,44,45,47,49,50,54,56,57,63,64,66,68,74,84}.

For statistical analyses and methods used to identify risk or protective factors for lean NAFLD or fatty liver, studies most often completed comparisons of characteristics among various study groups and/or adjusted multivariate models to identify the degree of association between dietary or physical activity risk factors and NAFLD risk or prevalence. In these adjusted models, some studies accounted for minimal confounding variables such as age, sex, and

anthropometric measures^{9,35,41,47,54–56,84,86} while some studies utilized multiple models to account for a comprehensive list of confounding variables related to socioeconomic status, lifestyle, medical history, dietary habits, and anthropometrics^{18,27,38,44–46,48,49,51–53,59–62,71–73,75–83}.

3.2 Key Terms and Definitions

The key terms used to identify and define body weight status, NAFLD, and excessive alcohol intake varied significantly. The most common terms utilized to categorize weight status in the population of interest were lean, normal weight, or non-obese. Twenty-three studies followed ethnicity-specific BMI parameters that defined lean as BMI < 23 kg/m² in Asian populations and BMI < 25 kg/m² for non-Asian populations^{20,27,28,30,31,34,36,40–42,45,46,58,69,72–75,78,79,85,86}. However, other studies were more varied in the terminology and definitions used. Four studies utilized lean and non-obese interchangeably and defined the population as BMI < 25 kg/m²^{9,10,70,85}. Five studies conducted in Asia did not utilize ethnicity-specific BMI parameters and defined its populations as lean based on BMI < 25 kg/m²^{9,47,48,81,84}. Ten studies combined lean and overweight individuals and identified them as non-obese based on a BMI < 25–28 kg/m², suggesting that these two weight categories did not need to be distinguished from each other^{39,44,52,53,56,57,63,65,66,71}. Finally, 23 studies either did not use any terminology or anthropometric measures to categorize body weight in the study population or used terms such as lean or non-obese without providing BMI or WC parameters as definitions^{18,29,32,33,35,38,43,49–51,54,55,59–62,64,68,76,77,80,82,83}. Waist circumference parameters were less frequently specified in the research, but among those that provided definitions, the parameters indicating normal weight or no abdominal adiposity ranged from ≤ 80–102 cm (males) and ≤ 80–90 cm (females)^{33,33,40,42–44,47,48,57,63,67,69,75,76,82,86}.

The most common terms used in the literature to classify liver health ranged from being very specific such as NAFLD or NASH to using more general terms such as fatty liver. Thirty-nine studies explicitly identified participants as having NAFLD, three studies identified participants as having NASH^{30,31,64}, and one study identified participants as having MAFLD⁷⁵. The remaining 21 studies did not specify if participants had NAFLD and referred to participants as having hepatic steatosis, hepatocellular injury, fatty liver, or Fatty Liver Disease^{28,29,32–39,42,50,51,54–58,61,67,68}. While 67% of the studies utilized abdominal ultrasound as a method to diagnose NAFLD or fatty liver in participants, several other methods were utilized in less frequent amounts. These methods included participant self-report^{27,81}, CT scan^{10,18,29,66}, MRI^{32,39}, ultrasound elastography³⁰, Proton Magnetic Resonance Spectroscopy (H-MRS)³⁹, measuring serum liver enzymes^{28,35–37,50,55}, or utilizing various prediction equations including Fatty Liver Index (FLI), Hepatorenal Index (HRI), and NAFLD Liver Fat Score^{33,36,38,43,83}. Four studies utilized liver biopsy to diagnose NAFLD, which is considered the gold standard for diagnosing this condition^{30,31,64,66}.

In addition to variability in the terms utilized to classify liver health, NAFLD diagnostic criteria were inconsistent. Thirty-three studies provided no NAFLD diagnostic criteria beyond identifying fatty liver using imaging (i.e., ultrasounds, CT, or MRI) or predictive equations. While some of these studies excluded participants for reasons that could be related to ruling out secondary causes of liver disease, authors did not explicitly state that this was the purpose of the exclusion criteria^{9,18,20,28,32,34–37,39,40,42,45,50–58,61,65–69,74–76,84,86}. In contrast, 14 studies required participants met more extensive list of criteria including no excessive alcohol intake, use of hepatotoxic medications, and secondary causes of liver disease including hepatotoxic drugs, history of autoimmune liver disorders, hereditary conditions, HBV or HCV infections, cancer,

hyperthyroidism, and chronic diseases known to increase risk for NAFLD including DM, HLD, CVD, and MetS^{31,41,44,46,47,49,59,60,63,64,70,75,83,85}. The remaining studies implemented a diagnostic criteria that ruled out select secondary causes of liver disease such as excessive alcohol intake and viral hepatitis, but the exclusion list was not extensive^{10,27,30,33,38,43,48,62,65,71–73,77–82}.

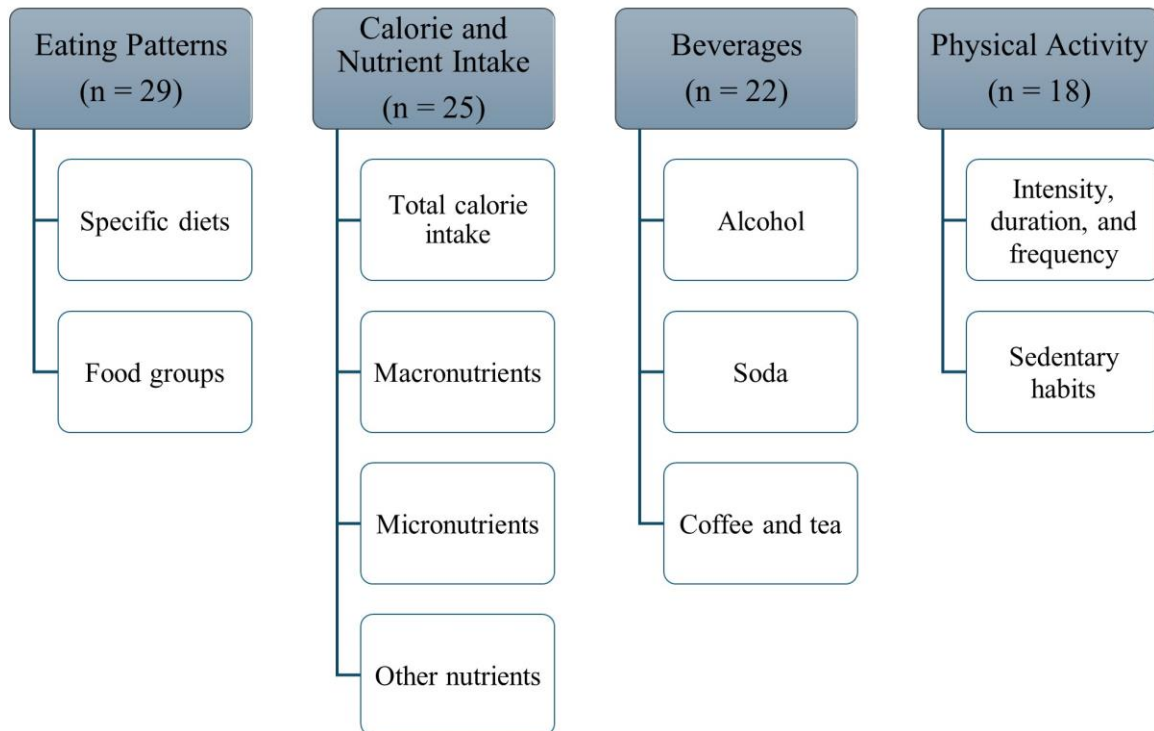
Although excessive alcohol intake is a more common factor to be identified as a secondary cause of liver disease, specifications on acceptable alcohol intake was also a source of variance in the body of evidence. Nineteen studies did not provide parameters for excessive alcohol intake^{32–36,38,40,42,43,51,54,56–58,61,66–68,75}. Among the remaining studies, the most common specifications for daily excessive alcohol intake were > 30–40 g/day (males) and > 20–30 g/day (females)^{9,10,29–31,41,45–49,52,53,59,60,64,65,69,81}. The most common definition of excessive alcohol intake based on weekly intake was > 210 g/week (males) and > 140 g/week (females), but authors did not specify if alcohol intake patterns (i.e., number of drinks consumed in a single sitting) were considered^{27,72,73,77–79}. Other studies defined excessive alcohol intake using lower parameters including > 20 g/day (males) and > 10 grams/day (females)^{20,37,44,63} and $\geq$ 140 g/week (males) or $\geq$ 70 g/week (females)^{50,70,71,74,82,83}. Additionally, four studies excluded participants with any alcohol intake prior to the study^{62,80,84,86} while two studies utilized more vague terms and excluded participants with a history of “alcohol dependency”^{28,55}.

3.3 Dietary and Physical Activity Research Topics

Studies included in this scoping review examined a broad range of topics related to dietary and physical activity risk and/or protective factors for lean NAFLD. These topics examined the association between specific diets, food groups, macronutrients, micronutrients, beverages, and various physical activity characteristics and lean NAFLD. Figure 3.3 provides a

graphical overview of the topics and subtopics included in the body of evidence. Subsections 3.4 through 3.7 summarize key results reported under each main topic and their associated subtopics.

Figure 3.3. Dietary and Physical Activity Research Topics



3.4 Eating Patterns and Lean NAFLD

A total of 29 articles studied dietary risk factors related to eating patterns and lean NAFLD risk. The predominant study designs were cross-sectional (n = 14) and prospective (n = 10). The remaining articles were matched case-control (n = 2), pre and post intervention (n = 2), and retrospective (n = 1) studies. The sample sizes ranged from 12 participants in an intervention study to 77,795 participants in a large prospective study. Sixteen studies examined the effects of common dietary patterns including vegetarian (n = 2), gluten free diet (n = 3), DASH (n = 2), Mediterranean (n = 3), high-protein low carbohydrate (n = 1), high carbohydrate low protein (n = 1), low-refined carbohydrate (n = 1), and low fat (n = 1). An additional five studies reported on

NAFLD risk and unspecified diets characterized by varying composition of animal and plant-based foods. Seventeen studies examined the association between the intake of different food groups including fruits, vegetables, whole grains, ultra-processed foods, and red meat and NAFLD risk in lean populations. Due to the heterogeneity in study designs and topics, studies were categorized based on whether they examined specific diets or focused on the association between the intake of plant-based foods, animal-based foods, and/or miscellaneous food groups and lean NAFLD risk. Detailed data are shown in Table 3.1.

Diets

Two studies analyzed the association between vegetarian diets and NAFLD risk in lean populations and found opposing results. A cross-sectional study conducted in South Korea observed no significant difference in NAFLD prevalence between vegetarian and non-vegetarian groups (29.9% vs 25.0%, $p = 0.055$)⁴⁷. In contrast, a cross-sectional study conducted in Taiwan observed a significant inverse association between vegetarian diets and NAFLD risk (OR = 0.79) in males and females. However, further adjustment for BMI attenuated the protective effect of vegetarian diets and it was no longer significant (OR = 1.05, 95% CI: 0.89–1.25)⁸⁶.

Two studies examined the association between DASH diet adherence and NAFLD risk in lean populations. Both were cross-sectional studies based in China and observed a significant inverse association between DASH diet adherence and NAFLD or MAFLD risk. The association was especially pronounced in lean participants as compared to obese participants. The ORs comparing highest to lowest quintile of DASH diet adherence were 0.70–0.76 (lean participants) and 0.90–0.94 (obese participants)^{75,76}. One of the studies also noted a difference among sexes, where DASH diet was inversely associated with NAFLD in females (OR = 0.71) but not in males (OR = 0.90, $P_{\text{trend}} = 0.443$)⁷⁶.

Three studies examined the effect of Mediterranean diet on NAFLD or MAFLD risk in lean populations. Two studies based in China observed no association between Mediterranean diet adherence (adapted for non-Greek populations) and NAFLD or MAFLD risk in lean participants. The ORs comparing highest to lowest levels of Mediterranean diet adherence were 1.03 (MAFLD risk) and 0.88 (NAFLD risk)^{69,75}. In contrast, a prospective study involving a lean Swiss population reported a significant inverse association between Mediterranean diet adherence and HS based on FLI to identify fatty liver (RR = 0.50). The association was weakened, yet still significant after the model was adjusted for BMI and WC (RR = 0.60–0.61). No significant association between Mediterranean diet adherence and HS risk was observed when NAFLD liver fat score was used to identify fatty liver³⁸.

Three studies examined the association between GFD and NAFLD risk in lean individuals. All were all conducted in Italy^{40–42}. Two studies reported a significant association between GFD and increased NAFLD risk among lean participants with CD^{40,41}. A retrospective study reported HS prevalence significantly increased among participants following a GFD after a median follow up of seven years (prevalence rates increased from 1.7% to 11.1%, $p < 0.0001$)⁴⁰. A case-control also reported a GFD was associated with higher NAFLD risk (OR = 2.90) in the CD group and the relative risk for NAFLD was significantly higher risk in the CD group following GFD compared to the general population (RR = 5.71)⁴¹. In contrast, a small prospective study reported a non-significant increase in HS prevalence rates in lean individuals with CD who followed a GFD for one-year (prevalence rates increased from 18% to 28.5%, $p = 0.1$)⁴².

Three studies examined the effects of diets with varying levels of food groups including animal proteins, vegetables (non-starchy and starchy), fruit, and refined and complex

carbohydrates^{48,77,79}. These diets were labeled as high inflammatory potential, rice-rich, sugar-rich, or animal foods rich diets. Results from three studies indicated that diets composed of high animal proteins (red meat, poultry, fish, organ meats) and refined grain products (snack foods, instant noodles), and lower in starchy and non-starchy vegetables were a risk factor for NAFLD in lean participants. Two large prospective studies observed a positive association between these types of diets and NAFLD risk (HR = 1.11–1.22), while a cross-sectional study observed a significant interaction between a high noodle/meat diet and genetic factors known to increase NAFLD risk ($P_{\text{interaction}} = 0.031$)^{48,77,79}. However, the cross-sectional study did not observe a significant interaction between genetic traits and other types of diets that were also characterized by either moderate or high intake of animal proteins and/or refined grains ($P_{\text{interaction}} = 0.088–0.814$)⁴⁸.

Finally, two intervention studies assessed the effects of diets with manipulated macronutrient composition on indicators of fatty liver in lean populations. Results indicated that short term manipulation of the types of carbohydrates or the percentages of calories from the three macronutrients did not significantly affect indicators of fatty liver^{28,39}. A small, quasi-experimental study conducted in the USA that compared the effects of a high fruit and vegetable diet or a high fruit and vegetable diet combined with either a low refined carbohydrate diet or a low-fat diet on biomarkers of NAFLD. Results indicated there was no significant effect of any of the diets on AST and ALT. The diets involving low refined carbohydrates and low fat were associated with a significant reduction in ceramides (reduction from 64% to 29%, $p < 0.05$). However, researchers could not draw direct conclusions about the effects of these diets on NAFLD risk because ceramides are also biomarkers for other metabolic diseases such as metabolic syndrome and T2DM²⁸. A small single-blind parallel study in the Netherlands

compared the effects of a high protein-low carbohydrate (HPLC) and high-carbohydrate-low protein (HCLP) diets on intrahepatic triglycerides (IHTG). After the 12 week intervention, there were no significant changes in IHTG in either diet groups and there were no significant differences in IHTG when comparing the two groups³⁹.

Plant-Based Food Groups

Multiple studies evaluated different plant-based foods including vegetables, fruit, whole grains, legumes, and nuts. Vegetable intake was the most frequently studied food group in this category with a total of seven studies on this topic^{60,70–72,74,76,77,84}. Three studies identified results indicative of no association between total vegetable intake and NAFLD risk^{60,76,77}. Two of these studies included a prospective study conducted in China that identified a non-significant inverse association between high vegetable intake and NAFLD risk (HR = 0.96), and a smaller cross-sectional study that reported no significant association between two different measures of vegetable intake in males and females (OR = 0.76–0.81)^{60,77}. One matched control study was more inconclusive regarding vegetable intake and NAFLD risk as lean NAFLD participants had lower vegetable intake than obese controls and obese NAFLD groups ($p < 0.05$), but intake did not differ from lean controls⁷⁰.

Five studies examined specific types of vegetables^{60,71,72,74,84}. Two cross-sectional studies based in China observed an inverse association between green vegetables intake and NAFLD risk in lean participants but not obese participants (OR = 0.72–0.77)^{71,72}. A cross-sectional study in China observed that consuming ≥ 100 grams of tubers weekly was associated with decreased NAFLD risk in lean participants (OR for training set = 0.506, OR for validation set = 0.663)⁷⁴. In contrast, another cross-sectional study reported intake of green and yellow vegetables was inversely associated with NAFLD prevalence among females in the fully adjusted logistic

regression model, though the ORs for NAFLD did not reach significance when examining higher quartiles of intake (ORs for increasing intake = 1.35, 1.09, and 0.54, $P_{\text{trend}} = 0.04$)⁶⁰. Two studies based in China and Iran reported that potato intake may be associated with NAFLD risk based on comparisons between lean controls and lean NAFLD groups^{70,84}. The study conducted in Iran further observed an association between a one gram increase in potato intake and a 2.5 time increase in NAFLD risk in lean participants (OR = 2.58)⁸⁴.

Four studies evaluated fruit intake and NAFLD risk in lean populations^{33,60,70,76,86}. Two cross-sectional studies (based in Taiwan and Japan) reported no association between fruit intake and NAFLD risk (OR = 1.02, 95% CI 0.96–1.08 and OR = 0.68–0.82, $P_{\text{trend}} = 0.12$ –0.60) after adjusting statistical models for BMI^{60,86}. This corresponded with findings in a Chinese cross-sectional study that observed no difference in fruit intake between non-NAFLD and NAFLD groups composed of lean individuals⁷⁶. In contrast, one cross-sectional study conducted in China observed high fruit intake may be possibly associated with NAFLD risk due to lean NAFLD participants consuming significantly higher amounts of fruit compared to lean and obese controls ($p < 0.05$ for all comparisons)⁷⁰. A Finnish prospective study reported the opposite in that lower fruit intake may be associated with NAFLD risk due to a fatty liver group having lower fruit intake compared to a group without fatty liver ($p = 0.023$)³³.

Other plant-based food groups studied included rice, noodles, whole grains, unspecified grains, nuts, and legumes^{55,59,76,84}. Two cross-sectional studies in Japan reported significant positive association between higher rice intake and NAFLD prevalence (OR = 1.498–1.87). One study observed this association in females, but not in males while the other cross-sectional study only involved male participants and thus intake could not be compared to females^{55,59}. In contrast, a cross-sectional study based in Iran reported potentially no association between rice

intake and NAFLD risk in lean males and females. This conclusion was based on there being no significant difference in rice intake when comparing the lean NAFLD group to lean controls, obese controls, and obese NAFLD groups⁸⁴. Similar patterns were seen with noodle intake where one cross-sectional study observed a positive association with indicators of fatty liver (ALT and GGT, OR = 1.422–1.467) while another cross-sectional study observed no association^{55,59}.

Six studies examined the influence of other grain products on NAFLD risk in lean populations^{18,59,70,76,84,86}. Four studies explored the association between unspecified grain products and NAFLD risk. Three cross-sectional studies observed no association with NAFLD risk^{59,76,84}, while a matched case-control observed a potential association with increased NAFLD risk based on a study group comparison where lean NAFLD participants consumed more total grains than lean controls and the same amount as obese controls ($p < 0.05$ for both comparisons)⁷⁰. Two studies observed an inverse relationship between whole grain intake and NAFLD risk (OR = 0.75–0.96)^{18,86}, though one study reported the inverse association was no longer significant after adjustment for BMI (OR = 0.99, 95% CI: 0.96–1.01)⁸⁶.

Finally, two studies evaluated the relationships between intake of nuts and legumes and NAFLD risk using study group comparisons. A cross-sectional study observed a potential association between lower nut and legume intake and increased NAFLD risk as evidenced by lean NAFLD participants having lower intake of nuts and legumes compared to lean participants without NAFLD ($p = 0.024$)⁷⁶. In contrast, a matched case-control study observed similar nut intake between lean NAFLD participants and lean controls and obese NAFLD participants⁷⁰.

Animal-Based Food Groups

A total of eight studies examined the association between lean NAFLD risk and animal-based foods including red meat, poultry, fish, eggs, and milk^{9,27,70,73,76,84,86}. One study reported a

positive association between total meat intake and NAFLD risk (OR = 1.09), though this association was no longer significant after adjustment for BMI (OR = 1.04, 95% CI: 0.95–1.14)⁸⁶. Four additional studies examined the effects of red meat on NAFLD risk^{27,73,76,84}. Two large prospective studies (based in China and United States) reported positive association between red meat intake and NAFLD risk (HR = 1.11–1.80), but the study based in the United States reported the association was no longer significant after adjustment for BMI (HR = 0.95–1.12, $P_{\text{trend}} > 0.05$)^{27,73}. In contrast, two cross-sectional studies observed a possible no association between red meat intake and NAFLD based on a risk analysis (OR = 0.99, p value = 0.72) and a comparison among study groups where there was no significant difference in red meat intake between lean non-NAFLD and NAFLD groups^{76,84}.

Among studies examining the association between lean proteins and NAFLD risk, one study evaluated poultry intake and four studies evaluated fish intake^{9,27,84,86}. The one study examining poultry intake found no association between intake and lean NAFLD incidence after the model was adjusted for BMI (HR = 1.08, $P_{\text{trend}} = 0.397$)²⁷. Three studies reported no association between fish intake and NAFLD risk (HR = 1.01, 95% CI: 0.91–1.12; HR = 1.08, $P_{\text{trend}} = 0.718$, OR = 1.00, p value = 0.46)^{27,84,86}. In contrast, a small cross-sectional study observed intake of fish and fish products ≥ 4 times/week was associated with reduced NAFLD risk in lean participants (OR = 0.261)⁹.

Three studies examined the association between NAFLD risk and milk and eggs^{70,76,84}. All three studies used study group comparisons and observed no difference in dairy and/or egg intake between lean NAFLD participants and lean controls with NAFLD, obese controls, and/or obese NAFLD participants^{70,76,84}. One study used a logistic regression analysis and reported no significant association between dairy intake and NAFLD risk (OR = 1.00, p-value = 0.80)⁸⁴.

Miscellaneous Food Groups

Five studies explored the association between intake of ultra-processed foods, fried foods, fast food and/or oil and NAFLD risk^{9,74,78,84,85}. Two studies observed ultra-processed foods intake were likely associated with NAFLD risk in lean individuals. One large prospective study observed a significant association between increasing ultra-processed foods intake and NAFLD risk (HR = 1.18) and a small cross-sectional observed lean NAFLD participants consumed significantly more processed foods than lean participants without NAFLD ($p = 0.003-0.046$)^{9,78}. A total of two studies also examined the association between fast food intake and NAFLD^{84,85}. One study reported no association between fast food and NAFLD risk based on a logistic regression analysis (OR = 0.99, p value = 0.42)⁸⁴. The second study used group comparison and observed lean NAFLD participants consumed less fast food than obese NAFLD ($p = 0.004$). However, there were no other comparison groups such as lean or obese participants without NAFLD to fully explore the association between fast food intake and lean NAFLD⁸⁵. Three studies examined the association between oil intake and NAFLD risk, though only one of these studies specified the types of oils examined^{9,84,85}. Two studies reported no association between total oil intake and NAFLD risk based on a logistic regression risk analysis (OR = 1.01, p value = 0.35) and a comparison of dietary habits among study groups, which observed no difference in the monthly use of cooking oil between lean NAFLD and obese NAFLD groups ($p = 0.287$)^{84,85}. A small cross-sectional study comparing different types of oil intake among study groups observed that lean NAFLD participants consumed olive and canola oil less frequently (number of times per week) compared to lean participants without NAFLD ($p = 0.031$)⁹. Finally, one study examined the association between fried food and lean NAFLD and observed an intake

of ≥ 50 grams of fried food weekly was significantly associated with NAFLD risk in lean participants (OR = 1.778–2.246)⁷⁴.

Table 3.1 Risk and protective factors related to eating patterns in lean NAFLD or fatty liver

Author	Study Design	Participant Characteristics	Weight Terminology	NAFLD diagnostic criteria	Main Findings
Chiu et al ¹⁸⁶ 2018 Taiwan	Cross-sectional	Total sample = 3400 Data categorized as non-vegetarian and vegetarian Mean age 54-55 years 33.9% male	Normal weight defined as BMI < 24 kg/m ² . Abdominal adiposity as WC ≥ 90 cm (males) and ≥ 80 cm (females).	Abdominal US No NAFLD diagnostic criteria specified. Participants excluded from study for following reasons: (1) current alcohol drinker, (2) current smoker, (3) current or past history of HBV or HCV, (4) history of cancer	• Vegetarian diet inversely associated with NAFLD risk, but no longer significant after adjustment for BMI OR = 1.05, 95% CI: 0.89-1.25 • In stratified analysis, vegetarian diet inversely associated with NAFLD risk in participants with BMI < 24 kg/m² but not significant OR = 0.91, 95% CI = 0.75-1.11 • Higher intake of meat, fish, and fruits positively associated with NAFLD risk, but association no longer significant after adjustment for BMI Meat OR = 1.04, 95% CI: 0.95-1.14 Fish OR = 1.01, 95% CI: 0.91-1.12 Fruit/fruit juice OR = 1.02, 95% CI: 0.96-1.08 • Whole grain intake inversely associated with NAFLD risk, but no longer significant after adjustment for BMI OR = 0.99, 95% CI = 0.96-1.01
Choi et al ⁴⁷ 2015 South Korea	Cross-sectional, retrospective	Total sample = 1230 Participants categorized as vegetarian or non-vegetarian Mean age 48 years 61.2% male	Normal weight defined as BMI 18.5-24.9 kg/m ² . Abdominal adiposity defined as WC ≤ 90 cm (males) or ≤ 80 cm (females)	Abdominal US NAFLD diagnostic criteria: Fatty liver verified by US in the absence of (1) excessive alcohol intake >30 g/d (males) and >20 g/d (females), (2) positive biochemical tests for HBV or HCV (3) known etiologies of liver disease, (4) steatogenic medications	• Vegetarian diet does not protect against NAFLD • No significant difference in NAFLD prevalence between vegetarian and non-vegetarian group (29.9% vs 25.0%, p = 0.055)

Ciccone et al ⁴⁰ 2019 Italy	Retrospective Median follow up 7 years	Total sample = 185 Mean age 35 years 22.7% male	Normal weight defined as BMI 18.6-24.9 kg/m ² . Abdominal obesity defined as WC ≥ 94 cm (males) and ≥ 80 cm (females)	Abdominal US Evaluated non-alcoholic HS. Diagnosis occurred in GI clinic with no diagnostic criteria specified	- Gluten Free Diet (GFD) associated with increased risk for non-alcoholic HS in CD patients - HS prevalence increased from 1.7% at baseline to 11.1% of participants after following GFD, $p < 0.0001$ (based on median follow up of 7 years)
Deng et al ⁶⁹ 2021 China	Cross-sectional	Total sample = 2981 Data categorized by HLS (range 0-6). Mediterranean diet part of HLS Mean age 61 years 32% male	Normal weight defined as BMI 18.5-23.9 kg/m ² . Abdominal adiposity defined as WC ≥ 85 cm (males) or ≥ 80 cm (females)	Abdominal US NAFLD diagnostic criteria not specified Participants excluded from study for (1) history of malignancy, hyperthyroidism or viral hepatitis, (2) alcohol intake ≥ 30 g/d (males) or ≥ 20 g/d (females)	- No significant association between Mediterranean diet (adjusted for Chinese population) and NAFLD risk - Comparing highest to lowest HLS score: OR = 0.88, 95% CI: 0.74-1.03, $P_{trend} = 0.105$
Honarvar et al ⁸⁴ 2017 Iran	Cross-sectional	Total sample = 478 Data categorized as lean non-NAFLD, lean NAFLD, non-lean non-NAFLD, and non-lean NAFLD Median age 42 years 40.6% male	Lean defined as BMI < 25 kg/m ² . No definition for WC provided	Abdominal US NAFLD diagnostic criteria not specified Participants excluded from study for following reasons (1) DM, (2) pregnancy or given birth in past 6 months, (3) alcohol consumer	- No significant difference between four study groups and intake of bread, rice, oil, red meat, dairy, fish, and fast food - Obese NAFLD had higher potato intake than lean non-NAFLD ($p = 0.028$) - Lean NAFLD had higher total starchy foods intake than lean non-NAFLD ($p = 0.025$), but did not differ from obese non-NAFLD and obese NAFLD In adjusted logistic regression model (included all study groups, adjusted for BMI) - Potato intake positively associated with NAFLD risk (95% CI) OR = 2.58, p value = 0.008 - No association between total oil, red meat, dairy, fish, or fast-food intake and NAFLD risk (95% CI) Total oil OR = 1.01, p-value = 0.35 Red meat OR = 0.99, p value = 0.72 Dairy OR = 1.00, p-value = 0.80 Fish OR = 1.00, p-value = 0.46 Fast food OR = 0.99, p-value = 0.4

Iwata et al ⁵⁵ 2013 Japan	Cross-sectional	Total sample = 1809 Mean age 35 years 100% male	No specific weight terminology used. No BMI or WC parameters provided to categorize weights	Liver enzymes (AST, ALT, GGT) Evaluated “hepatocellular injury”. No NAFLD diagnosis specified. Participants excluded from study for history of (1) stroke, (2) ischemic heart disease, (3) chronic renal failure, (4) alcohol dependency diagnosed by psychiatrist (5) liver cirrhosis or cancer (6) HBV or HCV	Fully adjusted logistic regression identified: - Elevated ALT positively associated with instant noodle intake for lunch at work (comparing more frequent to seldom intake) OR = 1.467, 95% CI: 1.074-2.005 - Elevated GGT positively associated with instant noodle and rice balls for lunch at work (comparing more frequent to seldom intake) Instant noodle OR = 1.422, 95% CI: 1.018-1.985 Rice balls OR = 1.498, 95% CI: 1.022-2.195 - Elevated GGT and AST negatively associated with snacking during work (comparing more frequent to seldom intake) GGT OR = 0.544, 95% CI: 0.419-0.705 AST OR = 0.643, 95% CI: 0.478-0.864)
Khalatbari-Soltani et al ³⁸ 2020 Switzerland	Prospective study Mean follow up 5.3 years	Total sample = 2288) Data categorized by quintiles of MDS Mean age 56 years 34.6% male	No specific terminology or anthropometric parameters used to categorize weight	FLI and NAFLD Liver Fat Score Evaluated HS. FLI ≥ 60 and NAFLD liver fat score ≥ 0.640 diagnosed HS. FLI based on BMI, WC, TG, and GGT. NAFLD liver fat score based on presence of MetS, T2DM, and fasting insulin, AST, and AST/ALT ratio Limited details on participant exclusion criteria provided	- Increasing MDS adherence inversely associated with HS based on FLI (comparing Q5 vs Q1 of diet adherence) RR = 0.50, 95% CI: 0.28-0.91, P_{trend} < 0.006 - Inverse association between MDS adherence and HS weakened with adjustment for BMI and WC but still significant (comparing Q5 vs Q1 of diet adherence) BMI adjusted model RR = 0.61, 95% CI: 0.34-1.09, P_{trend} = 0.031 BMI + WC adjusted model RR = 0.60, 95% CI: 0.34-1.08), P_{trend} = 0.034 - No association between MDS and HS risk based on NAFLD liver fat score (comparing Q5 vs Q4 of diet adherence) RR = 0.96, 95% CI: 0.60-1.53, P_{trend} = 0.80

Kim et al ²⁷ 2022 USA	Prospective study Follow up every 4 years for duration of 20 years	Total sample: 77,795 Participants categorized by frequency of red meat consumption ranging from ≤ 1 serving/week to ≥ 2 serving/day Mean age 40-41 years 0% male	Lean defined as BMI < 25. No WC parameters provided	Participants self-reported NAFLD diagnosis NAFLD diagnostic criteria: Self-reported NAFLD diagnosis without presence of cirrhosis, HBV, or HCV Excluded participants with excessive alcohol intake (> 140 g/week) at baseline.	- Intake of total red meat, processed red meat, unprocessed red meat, and poultry positively associated with NAFLD risk (comparing frequencies of intake) Dose-dependent risk ratios (per 1 serving increase/day, 95% CI, $P_{\text{trend}} < 0.0005$) Total red meat HR = 1.31 Unprocessed red meat HR = 1.29 Processed red meat HR = 1.80 Poultry HR = 1.49 - All associations attenuated after model adjusted for BMI (based on dose-dependent risk ratios per 1 serving increase/day, 95% CI) Total red meat HR = 0.99, $P_{\text{trend}} = 0.855$ Unprocessed red meat HR = 0.95, $P_{\text{trend}} = 0.482$ Processed red meat HR = 1.12, $P_{\text{trend}} = 0.326$ Poultry = 1.08, $P_{\text{trend}} = 0.397$ - No significant association between fish intake and NAFLD risk (based on dose-dependent risk ratio per 1 serving increase/day, 95% CI) HR = 1.08, $P_{\text{trend}} = 0.718$
Li et al ⁷⁰ 2019 China	Matched case-control study	Total sample = 351 Data categorized by lean controls, lean NAFLD, obese controls, obese NAFLD Mean age 43-45 years 49% male	Lean and non-obese used interchangeably. Defined as BMI < 24 kg/m ² . Parameters for WC not provided	Abdominal US NAFLD diagnostic criteria: Abnormal US images indicating fatty liver without the following (1) alcohol intake >140 g/week (male) and >70 g/week (female), (2) infection with HBV, HCV, or dual HBV/HCV, (3) hepatolenticular degeneration, autoimmune diseases, (5) total parenteral nutrition within past 4 months, (6) hepatotoxic drugs intake, (7) malignancies, (8) DM, or (9) pregnancy	- Compared to lean controls, lean NAFLD had ($p < 0.05$ for all) Higher intake of grains, potatoes, fruit, poultry, and beans No significant difference in vegetable, fish, or red meat intake - Compared to obese NAFLD, lean NAFLD had ($p < 0.05$ for all) Lower intake of grains, potato, vegetables, red meat, and fruit No significant difference in fish or poultry intake - No significant difference in nuts, egg, and milk intake among all study groups

Li et al ⁷¹ 2021 China	Cross-sectional	Total sample = 26,891 Data categorized by GLV intake frequency (ranging from almost never to ≥ 7 x/week) Mean age 38-46 years 47.3% male	Combined normal weight and overweight participants. Referred to as non-obese. Defined as BMI < 28 kg/m ² . No WC parameters provided Note: all participants met scoping review's BMI and/or WC parameters for "lean"	Abdominal US NAFLD diagnostic criteria: Fatty liver identified by US without history of significant alcohol intake (>140 g/week males, >70 g/week females) Participants excluded from study for history of CVD, cancer, alcoholic fatty liver disease, or other liver diseases.	- In adjusted logistic regression models, GLV intake inversely associated with NAFLD risk in total sample (highest vs lowest intake frequency) OR = 0.72, 95% CI: 0.59-0.90, P_{trend} < 0.0001 - Inverse association no longer significant after model adjusted for BMI (highest vs lowest intake frequency) OR = 0.81, 95% CI: 0.63-1.05, P_{trend} = 0.19 - Adjusted model stratifying data by BMI, GLV was inversely related to NAFLD risk in lean participants, but not obese participants (comparing highest vs lowest intake frequency) Lean OR = 0.72, 95% CI: 0.54-0.97 Obese OR = 1.04, 95% CI: 0.65-1.65
Li et al ⁷² 2021 China	Cross-sectional	Total sample = 24,572 Data categorized by frequency of seaweed intake ranging from almost never to > 1x/week Mean age 41 years 47.4% male	Normal weight defined as BMI 18.5-23.9 kg/m ² . No WC parameters provided	Abdominal US NAFLD diagnostic criteria: Fatty liver on US and absence of the following: (1) weekly alcohol intake > 210 g (males) and > 140 g (females), (2) history of CVD, cancer, and/or other liver diseases prior to assessment	- In fully adjusted logistic regression model, seaweed intake inversely associated with NAFLD risk (comparing highest vs lowest intake frequency) OR = 0.84, 95% CI: 0.73-0.96, P_{trend} < 0.001 - In stratified analysis, seaweed intake inversely associated with NAFLD in non-obese participants (combined normal weight and overweight participants), but not obese (comparing highest vs lowest intake) Non-obese OR = 0.77, 95% CI: 0.66, 0.91 Obese OR = 1.02, 95% CI: 0.79, 1.33)
Li et al ⁷³ 2023 China	Prospective cohort study Median follow up 4.2 years	Total sample = 15,568 Data categorized into non-NAFLD or NAFLD groups, and tertiles of organ meat intake	No specific terminology used to categorize weight. Data stratified as BMI < 24 or ≥ 24 kg/m ² . No WC parameters provided	Abdominal US NAFLD diagnostic criteria: Fatty liver identified on US and absence of following (1) weekly alcohol intake ≥ 210 g (males) and ≥ 140 g (females),	In fully adjusted Cox regression model, organ meat intake positively associated with NAFLD risk HR = 1.11; 95 % CI 1.01-1.22, P_{trend} = 0.02 (comparing T3 to T1 for intake)

		Mean age 39-42 years 42.4% male		(2) chronic HBV or HCV, (3) use of long-term steatogenic drugs	Association independent of age, BMI, smoking status, drinking status, HLD, DM, and HBP
Lu et al ¹⁸ 2022 USA	Prospective cohort study 30 year study with follow up at year 7, 20, and/or 25	Total sample = 2,685 Data categorized by quintiles of magnesium (Mg) intake (Q1-Q5) Mean age 50 years 41.9% male	Normal weight used to classify weight but no BMI or WC parameters provided as definition	Non-contrast CT scan at 25 year follow up NAFLD diagnostic criteria not specified Participants excluded from study if the following were present during follow up (1) pregnancy, (2) self-reported liver disease (3) alcohol intake ≥ 14 drinks/week (males) or ≥ 7 drinks/week (females), (4) hepatotoxic medication use, or (5) HIV	In adjusted logistic regression model, whole grains intake inversely associated with NAFLD risk Q5 versus Q1 intake OR = 0.75, 95% CI: 0.50-1.13, $P_{trend} = 0.02$
Martens et al ³⁹ 2014 Netherlands	Randomized single-blind parallel intervention study 12 week duration	Total sample = 16 Data categorized based on intervention (1) Protein Low Carb diet (HPLC), (2) High Carb Low Protein (HCLP) Mean age 23-25 years 43.7% male	Non-obese defined as BMI $< 25 \text{ kg/m}^2$. No parameters provided for WC	MRI and H-MRS Measured IHTG. Unclear if part of NAFLD diagnosis. No NAFLD diagnostic criteria specified. Participants excluded from study for (1) smoking, (2) alcohol intake > 10 drinks/week, (3) use of medications or supplements other than oral contraceptives	After 12-week intervention: - No significant change in IHTG in diet groups (baseline vs. post-intervention) HPLC: 0.25 ± 0.20 vs 0.22 ± 0.11 HCLP: 0.38 ± 0.22 vs 0.43 ± 0.24 - IHTG did not differ between diet groups (HPLC vs HCLP) 0.22 ± 0.11 vs 0.43 ± 0.24, $P_{trend} = 0.055$
Mathews et al ²⁸ 2017 USA	Non-randomized, uncontrolled trial 8-week duration	Total sample = 30 Data categorized by diet interventions: (1) High fruit and vegetable (FRUVED) (2) High fruit and vegetable + low refined carbohydrate (FRUVED + LRC)	Normal weight defined as BMI $< 25 \text{ kg/m}^2$. No parameters provided for WC	AST, ALT, and ceramides Evaluated risk for metabolic disorders including NAFLD based on ceramide levels. No NAFLD diagnostic criteria specified	- No significant changes in AST or ALT in each of the intervention groups - FRUVED + LRC and FRUVED + LF groups associated with significant reduction in ceramides (decreased from 64% to 29%, $p < 0.05$) compared to FRUVED group - No change in ceramides in FRUVED group

		(3) High fruit and vegetable + low-fat (FRUVED + LF) Mean age 24 years 47.0% male		Participants excluded for (1) pregnancy, (2) exhibiting an eating disorder (3) treatment for drug or alcohol abuse within the past year, (4) psychiatric treatment within the previous year (5) antibiotics use in the last 3 months	
Pan et al ⁷⁴ 2020 China	Cross-sectional	Total sample = 2446 Data categorized into training set and validation set groups Median age 43-44 years 48% male	Low risk body weight defined as BMI < 23 kg/m ² and WC < 80 cm (all sexes)	Abdominal US NAFLD diagnostic criteria not specified. Participants excluded from study for history of (1) alcohol abuse defined as weekly intake > 140 g (males) and > 70 g (females) in past year, (2) other liver disease causes including autoimmune hepatitis or drug induced liver disease	Adjusted logistic regression model indicated: - Fried foods intake ≥ 50 g/week positively associated with NAFLD risk in both groups compared to lower intake Training set OR = 2.246, 95% CI = 1.559–3.237, p < 0.001 Validation set OR = 1.778, 95% CI = 1.297-2.438, p < 0.001 - Tuber intake ≥ 100 g/week negatively associated with NAFLD risk in both groups compared to lower intake Training set OR = 0.506, 95% CI = 0.351–0.731, p < 0.001 Validation set OR = 0.663, 95% CI = 0.462-0.868, p = 0.004
Park and Kang ⁴⁸ 2020 South Korea	Cross-sectional	Total sample = 27,374 Data categorized into groups with or without presence of genetic trait associated with NAFLD risk (minor allele haplotype 22q13 loci) Mean age 54-55 years 35.9% male	Lean defined as BMI < 25 kg/m ² . Abdominal obesity defined as WC > 90 cm (males) and > 85 cm (females)	Abdominal US NAFLD diagnostic criteria: Fatty liver confirmed on US in absence of alcohol intake >40 g/d (males) and >30 g/d (females) Participants excluded from study if “serious disease present”	- High noodle/meat dietary pattern significantly interacted with genetic trait associated with NAFLD risk P_{interaction} = 0.031 - No significant interaction between other common dietary patterns and genetic trait associated with NAFLD risk P_{interaction} = 0.252 (balanced dietary pattern) P_{interaction} = 0.088 (rice-rich dietary pattern) P_{interaction} = 0.814 (bread/fast food dietary pattern)
Sharma et al ⁸⁵ 2020 India	Prospective	Total sample = 100 Data categorized into non-overweight NAFLD and obese NAFLD groups	Lean, non-overweight, and non-obese used interchangeably. Defined as BMI < 23 kg/m ² . No WC parameters provided	Abdominal US NAFLD diagnostic criteria: Fatty liver with absence of (1) alcohol intake > 21 drinks/week (males) and >14	No significant difference in average cooking oil intake per person/month between lean NAFLD and obese NAFLD groups (p = 0.287)

		Mean age 38-40 years No details provided on sex distribution		drinks/week (females) in past 2 years, (2) use of steatogenic medications, (3) certain hereditary disorders like abetalipoproteinemia, lecithin-cholesterol acyltransferase deficiency, cholesterol ester storage disease and Wolman's disease	Obese NAFLD with higher fast-food intake compared to lean NAFLD ($p = 0.004$)
Tajima et al ⁵⁹ 2017 Japan	Cross-sectional	Total sample = 2444 Data categorized by quartiles of rice, noodle, and bread intake (Q1-Q4) Mean age 52-53 years 40% male	No specific terminology or BMI and WC parameters provided to categorize weight	Abdominal US NAFLD diagnosis based on assumption that fatty liver was related to NAFLD due to participants being excluded from study for (1) alcohol intake ≥ 30 g/d (males) and ≥ 20 g/d (females), (2) self-reported possibility of pregnancy, (3) other self-reported liver diseases, (4) positive or unknown hepatitis B or C serology, (5) history of gastrectomy, (6) use of medication for HLD or DM, (7) use of breast cancer medications, (8) use of hormone replacement therapy, (9) T2DM	In fully adjusted logistic regression: - Rice positively associated with NAFLD prevalence in females but not males (comparing Q4 to Q1 intake) Females OR = 1.87, 95% CI: 1.03-3.41, $P_{trend} = 0.006$ Males OR = 1.29, 95% CI: 0.80-2.08, $P_{trend} = 0.12$ - No association between bread or noodle intake and NAFLD prevalence in both sexes (comparing Q4 to Q1 intake) Bread Females OR = 1.05, 95% CI: 0.56-1.97, $P_{trend} = 0.81$ Males OR = 0.78, 95% CI: 0.50-1.23, $P_{trend} = 0.31$ Noodle Females OR = 1.56, 95% CI: 0.87-2.80, $P_{trend} = 0.13$ Males OR = 1.41, 95% CI: 0.91-2.19, $P_{trend} = 0.046$
Tajima et al ⁶⁰ 2019 Japan	Cross-sectional	Total sample = 2444 Data categorized by quartile of fruit or vegetable intake Mean age 49-58 40% male	No specific terminology or BMI and WC parameters provided to categorize weight	Abdominal US NAFLD diagnosis based on assumption that fatty liver was related to NAFLD due to participants being excluded from study for (1) alcohol intake ≥ 30 g/d (males) and ≥ 20 g/d (females), (2) self-reported possibility of pregnancy, (3) other self-reported liver diseases, (4) positive or unknown hepatitis B or C serology, (5) history of	In fully adjusted logistic regression model: - No association between fruit intake and NAFLD prevalence (comparing Q4 to Q1 intake) Female OR = 0.82, 95% CI: 0.44-1.55, $P_{trend} = 0.60$ Male OR = 0.68, 95% CI: 0.42-1.11, $P_{trend} = 0.12$ - No association between total vegetable and other vegetable intake and NAFLD prevalence (comparing Q4 to Q1 intake) Total vegetable Female OR = 0.76, 95% CI: 0.40-1.45, $P_{trend} = 0.14$

				gastrectomy, (6) use of medication for HLD or DM, (7) use of breast cancer medications, (8) use of hormone replacement therapy, (9) T2DM	Male OR = 0.76, 95% CI: 0.40-1.45, $P_{\text{trend}} = 0.14$ Other Vegetables Female OR = 0.81, 95% CI: 0.42-1.53, $P_{\text{trend}} = 0.27$ Male OR = 0.79, 95% CI: 0.49-1.25, $P_{\text{trend}} = 0.43$ In females, linear inverse association between green and yellow vegetable intake and NAFLD prevalence but ORs not significant at higher quartiles of intake OR for Q1-Q4 = 1.00, 1.35, 1.09, 0.54, $P_{\text{trend}} = 0.04$
Tortora et al ⁴² 2015 Italy	Prospective Follow up at 6 and 12 months	Total sample = 98 Data categorized into HS or no HS at baseline Participants > 18 years Included both sexes, but no ratio provided	Normal weight defined as BMI 18.5-24.9 kg/m ² . Abdominal adiposity defined as WC $\geq$ 94 cm (males) and $\geq$ 80 cm (females)	Abdominal US Evaluated HS. Unclear if considered part of NAFLD diagnosis. Participants with T1DM and pregnancy were excluded from study	After following GFD for 1 year, HS prevalence increased from 18% to 28.5%, but change was not significant ($p = 0.1$)
Tovoli et al ⁴¹ 2018 Italy	Matched case control with prospective enrollment	Total sample = 404 Data categorized into control and CD group Median age 45-46 years 31% male	Lean defined as BMI < 25 kg/m ² . No WC parameters provided	Abdominal US NAFLD diagnostic criteria based on fatty liver confirmed on US in the absence of (1) alcohol intake > 30 g/d (males) and > 20 g/d (females), (2) HBV or HCV infections, (3) steatogenic medication use, (4) ongoing pregnancy, (5) any other liver damaging diseases including autoimmune or storage related	- In binary logistic regression, GFD associated with increased NAFLD risk in CD group OR = 2.90, 95% CI: 1.64-5.15, $p < 0.001$ - Relative risk for NAFLD significantly higher in lean CD patients compared to general population RR = 5.71, 95% CI: 2.30-14.19, $p < 0.001$
Yabe et al ⁹ 2023 Japan	Cross-sectional	Total sample = 169 Data categorized into non-obese NAFLD and non-NAFLD groups	Lean and non-obese used interchangeably. Defined as BMI < 25 kg/m ² . No WC parameters provided	Abdominal US, elastography, and/or self-report NAFLD diagnostic criteria not specified	Lean NAFLD group with less frequent intake of fish and fish products ($p = 0.004$) and olive oil or canola/rapeseed oil ($p = 0.031$) compared to non-NAFLD group

		Mean age 59-62 years 36.7% male		Participants excluded from study for (1) daily alcohol intake >30 g (males) or 20 g (females), (2) liver diseases including HCC, HBV, HCV, liver cirrhosis, PBC, primary sclerosing cholangitis, autoimmune hepatitis	- Lean NAFLD with more frequent intake of pastries and cake (p = 0.003), snack foods and fried sweets (p = 0.046), candy and caramels (p = 0.011), salty foods (p = 0.004), and pickles (p < 0.001) compared to non-NAFLD group. - More frequent fish and fish products intake inversely associated with NAFLD risk in lean NAFLD group OR for intake $\geq 4x/week$ = 0.261, 95% CI: 0.114-0.594, p = 0.001) - More frequent intake of pickles positively associated with NAFLD risk in lean NAFLD group OR for intake $\geq 4x/week$ = 2.880, 95% CI: 1.264-6.558, p = 0.012
Xie et al ⁷⁵ 2022 China	Cross-sectional	Total sample = 66,526 Data categorized into groups of non-obese non-MAFLD, non-obese MAFLD, obese non-MAFLD, and obese MAFLD. Further categorized by quintiles of increasing DASH or AMED (Adjusted Mediterranean diet) adherence (Q1-Q5) Mean age 49.5 years 37.4% Male	Lean defined as BMI < 24 kg/m ² . Overweight/non-obese defined as BMI < 28 kg/m ² . Abdominal adiposity defined as WC $\geq$ 90 cm (males) and $\geq$ 80 cm (females)	Abdominal US MAFLD diagnostic criteria: Fatty liver confirmed by US and presence of diabetes, overweight/obesity (BMI $\geq$ 23 kg/m ²), or two or more factors indicating metabolic risk including elevated WC, TG, FPG, HbA1c, blood pressure, or low HDL. Evaluation of alcohol intake not included in MAFLD diagnostic criteria. NAFLD diagnostic criteria not provided	In stratified analysis applying lean BMI definition: - DASH diet adherence inversely associated with MAFLD risk with more pronounced association in lean participants (Q5 vs Q4 of diet adherence) Lean OR = 0.76, 95% CI: 0.70-0.82, P_{trend} <0.001 Obese OR = 0.94, 95% CI: 0.81-1.09 - No significant association between AMED and MAFLD risk in lean and obese participants (Q5 vs Q4 of diet adherence) Lean OR = 1.03, 95% CI: 0.95-1.12, P_{trend} = 0.291 Obese OR = 0.98, 95% CI: 0.84-1.13, P_{trend} = 0.758
Xiao et al ⁷⁶ 2020 China	Cross-sectional	Total sample = 3051 Data categorized by quintiles of DASH diet adherence (Q1-Q5) Mean age 63-65 years	No specific terminology or BMI parameters to categorize weight. Abdominal obesity defined as WC $\geq$ 90 cm (males) and $\geq$ 85 cm (females)	Abdominal US No NAFLD diagnostic criteria specified. Participants excluded from study for the following (1) weekly alcohol intake > 14 drinks (males) and > 7 drinks	DASH diet adherence inversely associated with NAFLD in total sample, females, and lean participants (Q5 vs Q1) Total sample OR = 0.77, 95% CI: 0.61-0.97, P_{trend} = 0.009 Females OR = 0.71, 95% CI: 0.53-0.94, P_{trend} = 0.009

		31.7% male		(females), (2) self-reported viral hepatitis, (3) hospital confirmed malignancy, stroke, CAD, liver disease, renal failure, and/or physical and mental disability prior to study	Lean OR = 0.70, 95% CI: 0.51-0.96, $P_{\text{trend}} = 0.005$ - No association between DASH diet adherence and NAFLD in males and obese (Q5 vs Q1) Males OR = 0.90, 95% CI: 0.60-1.41, $P_{\text{trend}} = 0.443$ Obese OR = 0.90, 95% CI: 0.61-1.33, $P_{\text{trend}} = 0.736$ - When compared to non-NAFLD group, lean NAFLD had lower intake of nuts and legumes ($p = 0.024$) No difference in vegetable, fruit, dairy, whole grains/grain products, and red and processed meats
Zhang et al ⁷⁷	Prospective cohort study	Total sample = 17,360	No BMI or WC parameters provided to define lean	Abdominal US	In adjusted Cox regression model:
2021	Median follow up 4.2 years	Data categorized into quartiles of increasing dietary pattern adherence (Q1-Q4)		NAFLD diagnostic criteria: Fatty liver confirmed by US and absence of following (1) weekly alcohol intake > 210 g (males) and > 140 g (females), (2) other liver diseases including HBV, HCV, autoimmune liver disease, cirrhotic or liver cancer.	- Sugar-rich and animal-food rich diets positively associated with NAFLD risk in total sample (comparing Q4 vs Q1) Sugar-rich HR = 1.11, 95% CI: 1.01, 1.23, $P_{\text{trend}} = 0.03$ Animal-food rich HR = 1.22, 95% CI: 1.10, 1.36, $P_{\text{trend}} < 0.0001$ - No significant association between vegetable-rich diet and NAFLD risk (comparing Q4 vs Q1) HR = 0.96, 95% CI: 0.86, 1.07, $P_{\text{trend}} = 0.59$
China		Median age 37 years			In subgroup analysis stratified by sex:
		43% male			- Animal-food rich diet positively associated with NAFLD risk in males and females (comparing Q4 vs Q1) Female HR = 1.34, 95% CI: 1.12-1.60, $P_{\text{trend}} < 0.01$ Male HR = 1.17 (1.02, 1.33), $P_{\text{trend}} < 0.01$ - No association between sugar-rich diet and NAFLD risk in sexes except Q4 of diet adherence moderately associated with NAFLD risk in females HR for Q1-Q4 = 1.17, 1.10, 1.20, $P_{\text{trend}} = 0.04$

					No association between vegetable rich diet and NAFLD risk in all sexes Female HR = 1.03, 95% CI: 0.85-1.24, $P_{\text{trend}} = 0.9$ Male HR = 0.93, 95% CI: 0.81-1.07, $P_{\text{trend}} = 0.53$
Zhang et al ⁷⁸ 2022 China	Prospective study Median follow up 4.2 years	Total sample = 16,168 Data categorized by quartile of ultra-processed foods in g/1000 kcal/day (Q1-Q4) Mean age 38 years 42.6% male	No specific terminology used to categorize weight but based on stratified analysis, normal weight defined as BMI < 24 kg/m ² . No WC parameters provided	Abdominal US NAFLD diagnostic criteria: Fatty liver identified via US and absence of the following (1) weekly alcohol intake ≥ 210 g (males) and ≥ 140 g (females), (2) other liver diseases	- In fully adjusted Cox proportional hazard model, ultra-processed foods intake positively associated with NAFLD risk in total sample (Q4 vs Q1) HR = 1.18, 95% CI: 1.07-1.30, $P_{\text{trend}} < 0.0001$ - Stratified analysis showed no significant interaction between variables including sex and BMI and observed association
Zhang et al ⁷⁹ 2022 China	Prospective study Median follow up 4.2 years	Total sample = 12,877 Data categorized by quartile of dietary inflammatory potential score (Q1 = lowest inflammatory potential, Q4 = highest inflammatory potential) Median age 37 years 42% male	No specific terminology used to categorize weight but based on stratified analysis, normal weight defined as BMI < 24 kg/m ² . No WC parameters provided	Abdominal US NAFLD diagnostic criteria: Fatty liver via US and absence of (1) weekly alcohol intake ≥ 210 g/week (males) and ≥ 140 g (females), and (2) other liver diseases including HBV or HCV	- In fully adjusted Cox regression models, dietary inflammatory potential score positively associated with NAFLD risk (Q4 vs Q1) HR = 1.26, 95% CI: 1.13-1.41, $P_{\text{trends}} < 0.0001$ - Stratified analysis showed no significant interaction between risk factors including BMI and sex and observed association

3.5 Calorie Intake, Specific Nutrients, and Lean NAFLD

The topic of calorie, macronutrient, and micronutrient intake and lean NAFLD was explored by 25 studies. Study designs included cross-sectional (n = 14), prospective (n = 5), pre-post intervention (n = 2), and matched case control (n = 1). Total sample sizes ranged from 12 to 100,177 participants. Topics included calorie intake, carbohydrates, protein, fat, fat subtypes, vitamins, minerals, and other nutrients. Detailed data are shown in Table 3.2.

Calorie Intake

A total of eight studies examined the relationship between total calorie intake and NAFLD risk^{10,31,32,43,48,63,66,70}. Four other cross-sectional studies noted calorie intake was likely not associated with lean NAFLD risk based on there being no significant difference in total calorie intake between lean controls and lean participants with either NAFLD or NASH^{10,31,63,66}. These findings were also supported by a large cross-sectional study that observed no significant interaction between total calorie intake and genetic traits that are associated with increased NAFLD risk. A small randomized uncontrolled trial also observed no significant change in hepatic fat content despite a significant increase in caloric intake after the intervention ($p = 0.035$)^{32,48}. In contrast, one cross-sectional study indicated that higher calorie intake may be associated with NAFLD risk based on a study group comparison where lean NAFLD participants consumed significantly more calories than lean controls without NAFLD ($p < 0.05$)⁷⁰. A prospective study based in Italy noted that the timing of calories may be important based on an observation where higher calorie intake at dinner was associated with increased NAFLD incidence despite no differences in nutrient composition of dinners compared to lower tertiles of calorie intake (OR = 1.56)⁴³.

Carbohydrates

A total of 13 studies analyzed the association between carbohydrate intake and NAFLD in lean participants. Six studies observed a positive association between increasing carbohydrate intake and NAFLD risk or indicators of fatty liver in lean participants (OR = 1.005–2.22)^{10,48,50,59,64,84}. Some noteworthy findings included one cross-sectional study that identified increasing carbohydrate intake as an independent predictor of NAFLD prevalence (OR = 1.181, $P_{\text{trend}} = 0.023$) in lean participants, but not obese participants¹⁰. Another cross-sectional study observed that participants with a genetic trait associated with NAFLD risk and consumed a high carbohydrate diet (> 75% of calories from carbohydrates) had higher incidences of NAFLD compared to those with the same genetic trait consuming a low carbohydrate diet (defined as $\leq$ 75% of calories from carbohydrates, $p < 0.001$ for group comparison)⁴⁸.

Other studies utilizing study group comparisons reported less consistent results about the association between carbohydrate intake and NAFLD risk^{30,31,44,50,63,65,66,70,84}. Five studies observed results indicative of no association between carbohydrate intake and NAFLD risk. This was based on no significant difference in total carbohydrate between lean controls and participants with lean NAFLD or NASH^{31,44,63,66,84}. However, some of these studies also compared lean NAFLD to non-lean NAFLD or NASH participants and observed lean NAFLD participants either had lower carbohydrate intake ($p = 0.0456$) or did not differ in intake from the non-lean groups^{31,66,84}. Another study comparing lean NASH participants to non-lean NASH participants also observed no difference in percent of calories from carbohydrates between the groups, but none of the groups consumed excessive carbohydrate percentages compared to the reference range ($< 55\%$ of calories from carbohydrates). There were also no control groups without NASH to provide better comparison³⁰. Two other studies observed results that suggested

lower carbohydrate diets were associated with increased NAFLD risk^{50,65}. A small cross-sectional study observed that participants with NAFLD and a genetic trait associated with increased NAFLD risk consumed less carbohydrates compared to a group of participants with the genetic trait but without NAFLD ($p = 0.049$)⁶⁵. A large cross-sectional study concluded that the optimal carbohydrate intake for the study population was 50-60% of calories from carbohydrates and individuals should avoid very low carbohydrates that provide 35-45% of calories from carbohydrates to reduce NAFLD risk based on two graphing models exploring the association between carbohydrate energy ratio and abnormal AST and ALT levels⁵⁰.

Four studies evaluated the effects of simple carbohydrates and NAFLD or fatty liver risk^{32,36,44,64}. Two cross-sectional studies observed no significant difference in simple carbohydrate intake between lean NAFLD or NASH participants and lean groups with either no NAFLD or simple hepatic steatohepatitis^{44,64}. A randomized uncontrolled intervention trial and cross-over intervention trial also observed no significant effect of diets with varying levels of fructose and/or glucose on indicators of fatty liver including liver enzymes, FLI, HRI, and hepatic fat content based on MRI imaging^{32,36}.

Protein

A total of 13 studies explored the topic of protein and NAFLD risk. Three cross-sectional studies conducted in Asia reported no significant association between protein intake and NAFLD risk in lean participants based on multivariate analysis with logistic regressions^{48,81,84}. Eight studies other studies observed no significant difference in protein intake between lean NAFLD and lean participants without NAFLD or fatty liver, suggesting that protein intake may not be associated with the development of fatty liver or NAFLD in lean populations^{10,31,34,44,63,65,66,84}. Some of these studies also compared protein intake between lean NAFLD participants and non-

lean controls, NAFLD, and/or NASH participants. However, the results indicated no difference in protein intake among these groups, and this is more suggestive of protein intake not being associated with the development of obesity rather than NAFLD risk^{10,30,31,66,84}. One study observed the percentage of calories from protein was lower in the lean NAFLD group compared to obese controls and NAFLD groups, but there was no lean control group without NAFLD to fully evaluate the implications of these finds³⁴.

Two studies reported results that contradict the general findings that protein intake is not associated with lean NAFLD risk^{64,70}. This included a small cross-sectional that observed lean NASH participants consumed less protein compared to lean individuals with simple hepatic steatosis ($p < 0.05$). Researchers also reported low protein intake was positively associated with NASH risk in lean participants, but this was not well supported by statistical evidence from the logistic regression ($OR = 0.959$, $p = 0.179$, 95% CI not provided)⁶⁴. Meanwhile, another small cross-sectional study noted lean NAFLD participants had significantly higher protein intake compared to lean controls ($p < 0.05$) and similar intake of protein compared to obese controls and obese NAFLD participants. This may suggest a potential association between protein intake and NAFLD risk in lean individuals⁷⁰.

Total Fat

A total of 11 articles examined the topic of total fat intake and lean NAFLD risk. Four studies observed a potential association between increasing total fat intake and NAFLD risk^{30,65,70,84}. Two cross-sectional studies observed a significant association between total fat intake and NAFLD risk using either logistic regression ($OR = 1.023$) or an analysis of nutrient interactions with NAFLD in participants with genetic factors associated with NAFLD risk ($P_{\text{interaction}} = 0.006$)^{65,84}. Studies involving group comparisons and observed no difference in total

fat intake was comparing lean NAFLD participants and lean participants with NAFLD also suggest a potential association between increasing fat intake and NAFLD risk ($p = 0.001$ to $p < 0.05$)^{65,70}. Interestingly, an additional study based in Mexico observed lean NASH participants had higher percentage of calories from fat compared to overweight and obese NASH participants (42.0% vs 27.8–31.3%). This potentially suggests higher fat intake is associated with lean NASH and not overweight/obese NASH, but no definitive conclusions could be drawn because there was no lean control group without NASH to serve as comparison³⁰.

In contrast, seven studies reported potentially no association between total fat intake and NAFLD risk^{10,31,44,48,63,64,84}. Another cross-sectional study exploring nutrigenetic factors related to NAFLD risk reported no significant interaction between low or high fat intake (defined as $< 15\%$ or $>15\%$ of calories) and genetic traits that influence NAFLD risk⁴⁸. Additionally, five studies using study group comparisons observed no significant difference in total fat intake between lean NAFLD or NASH participants and lean controls without NAFLD or NASH^{10,31,44,63,64,84}. Some of these studies also compared intake between lean NAFLD and non-lean controls and/or non-lean NAFLD or NASH participants and observed no significant difference in total fat intake between these groups. This may suggest that other factors beyond fat intake influenced the development of lean NAFLD and yet protected the participants from developing obesity^{10,31,84}. In addition to these six studies, one study observed either no association or a negative association between fat intake and fatty liver risk. While an adjusted logistic model found no significant association between increasing proportion of calories from fat and abnormal AST and ALT, an adjusted Pearson's correlation analysis observed increased proportion of calories from fat was negatively associated with abnormal ALT and AST (correlation coefficients = -0.044 and -0.080 respectively). Additionally, a graphing model

comparing AST and ALT to percentage of calories from fat was U-shaped with the lowest enzyme levels occurring with 30–40% of calories from fat. Researchers concluded that an optimal calorie range for total fat intake for reducing NAFLD risk is 30–40%⁵⁰.

Fat Subtypes

Nine studies evaluated the association between lean NAFLD risk and fat subtypes including polyunsaturated fatty acids (PUFA), monounsaturated fatty acids (MUFAs), and saturated fatty acids (SFAs)^{10,44,62–66,81,84}. Some studies also examined PUFA:SFA ratio and specific types of PUFA including n-3s, n-6s, eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) and lean NAFLD^{62,64,65}. There was especially significant heterogeneity in results regarding the association between PUFA and NAFLD, while more consistent results occurred with studies examining MUFA and SFA intake. Nine studies examined PUFAs and/or specific types of PUFAs including n-3 PUFAs, n-6 PUFAs, EPA, and DHA^{10,44,62–66,81,84}. Two studies observed a positive association between increasing PUFA (total, n-3, and n-6 PUFAs) and NAFLD risk. These results were based on a logistic regression analysis (OR = 1.06) or analysis of interaction between PUFA intake and genetic traits associated with NAFLD risk ($P_{\text{interaction}}$ for total PUFA = 0.015, n-3 = 0.038, n-6 = 0.025)^{65,84}. On the other hand another cross-sectional study observed an inverse association between increasing intake of EPA or a combination of EPA + DHA and NAFLD risk (OR = 0.45–0.48)⁶². In contrast, one study reported that low total PUFA intake was potentially associated with increased lean NAFLD risk based on a study group comparison where lean NAFLD participants consumed significantly lower total PUFAs compared to lean controls ($p < 0.05$) and obese NAFLD groups ($p = 0.0195$)⁶⁶. However, a cross-sectional study reported no association between low PUFA intake and NAFLD risk, though these findings were not supported by statistical analysis⁶⁴. Finally, several studies

observed potentially no association between intake of PUFA (total, n-3, and n-6 PUFAs) and NAFLD risk based on study group comparisons and logistic regression analysis^{10,44,62–64,81}.

Eight studies examined the association between MUFA intake and NAFLD risk. Two studies reported no significant association between MUFA intake and NAFLD risk based on logistic regression analysis^{81,84}. Similar findings were also observed in five studies that compared MUFA intake between lean NAFLD or NASH participants and lean controls without NAFLD or NASH. There was no significant difference in intake between the study groups, suggesting potentially no association between MUFA intake and lean NAFLD risk^{10,44,63,64,66}. On the other hand, one small cross-sectional study reported significant interaction between MUFA intake and genetic traits that can influence NAFLD ($P_{\text{interaction}} = 0.002$). This finding was also supported by a group comparison where those with the genetic trait and NAFLD had higher intake of MUFAs compared to a group with the same genetic trait but without NAFLD ($p < 0.001$)⁶⁵.

Eight studies examined SFA and the majority of these studies observed no association between SFA intake and NAFLD risk in lean participants^{10,44,63–66,81,84}. Two studies using a logistic regression analysis observed no significant association between these two variables, while five additional studies reported no difference in SFA intake when comparing lean participants with NAFLD or NASH to lean participants without NAFLD or NASH^{10,44,63,64,66,81,84}. However, two studies observed findings that suggest a positive association between increasing SFA intake and lean NAFLD risk^{63,65}. One study reported a partial correlation coefficient that indicated SFA intake was positively associated with a biomarker for NAFLD in lean participants (coefficient = 0.379, $p = 0.03$)⁶³. Another study observed higher SFA intake in a group with NAFLD and genetic traits associated with increased NAFLD when compared to a group with the same genetic traits but without NAFLD ($p = 0.020$)⁶⁵.

Four studies examined topics related to the ratio of types of fats consumed^{10,44,64,65}. Two studies compared the PUFA:SFA ratio in lean participants with NAFLD or NASH and lean participants without either of these conditions. Both studies observed no significant difference in the PUFA:SFA ratios between these two groups^{44,64}. However, one of these studies also conducted a logistic regression analysis and reported that a low PUFA:SFA ratio was associated with NAFLD risk (OR = 2.951)⁶⁴. Two other studies also evaluated intake of vegetable and/or animal fats in lean participants, which have varying distributions of saturated and unsaturated fatty acids^{10,65}. One study reported higher vegetable intake in a group with NAFLD and genetic traits associated with NAFLD compared to a group with the same genetic traits but without NAFLD ($p = 0.002$). Researchers also observed a significant interaction between genetic traits influencing NAFLD risk and vegetable fat intake ($P_{\text{interaction}} = 0.017$)⁶⁵. Meanwhile, a cross-sectional study in South Korea observed no significant difference in vegetable fat and animal fat intake when comparing lean NAFLD participants to lean controls¹⁰.

Vitamins and Minerals

A total of 13 articles explored the topic of micronutrients and lean NAFLD risk. The micronutrients that were reviewed in the body of evidence included all fat-soluble vitamins, all B vitamins, vitamin C, sodium, potassium, calcium, phosphorus, iodine, iron, magnesium, manganese, choline, copper and selenium. However, the amount of literature and extent of analysis was minimal for most of these micronutrients. Most studies involved comparing intake between lean NAFLD and lean controls without NAFLD and lacked consensus.

Starting with micronutrients that were studied the most, four studies examined the association between sodium and NAFLD risk in lean individuals. Two large cross-sectional and prospective studies based in China reported a positive association between increasing sodium

intake and NAFLD prevalence (PR = 1.32 and HR = 1.19), though one study reported the positive association was attenuated and no longer significant after adjustment for BMI (PR = 1.06)^{46,80}. Studies using group comparisons for sodium intake provided conflicting results. When comparing between lean NAFLD and lean control groups, one study reported no difference in sodium intake while the second study reported lean NAFLD participants consumed significantly higher sodium intake ($p < 0.05$)^{10,70}.

Similar inconsistent results were observed in the three studies examining potassium and NAFLD^{10,46,70}. One large cross-sectional study reported a positive association between potassium intake and NAFLD prevalence in males, but not females (PR = 1.12 for males, PR = 0.97 for female)⁴⁶. Studies that used group comparisons observed that lean NAFLD participants consumed either the same amount or higher amount of potassium as lean controls^{10,46,70}. Only one study considered the influence of the ratio of sodium to potassium intake on NAFLD and found that a higher sodium to potassium ratio was positively associated with NAFLD risk in lean participants (PR = 1.13)⁴⁶.

Four studies analyzed the association between zinc intake and NAFLD risk^{63,64,70}. This included one small cross-sectional study that observed lower zinc intake in lean NASH participants compared to lean participants with HS. Researchers also reported low zinc intake was associated with lean NASH risk based on a logistic regression, though this was not well supported by statistical evidence (OR = 0.842, $p = 0.224$)⁶⁴. In contrast, study group comparisons suggested potentially no association between zinc intake and NAFLD risk as there was no significant difference in zinc intake between lean controls and lean NAFLD groups in two cross-sectional studies^{63,70}.

Iron intake was analyzed in four studies^{63,64,66,70}. A cross-sectional study in China reported lean NAFLD group had higher iron intake than lean controls ($p < 0.05$) and similar intake to obese controls and obese NAFLD groups⁷⁰. The remaining three studies found no difference in iron intake when comparing lean NAFLD or NASH participants with lean participants without NAFLD or NASH^{63,64,66}.

Three studies examined vitamin A intake and NAFLD risk by comparison of intake between lean NAFLD and other study groups^{10,44,70}. Two cross-sectional studies observed significantly lower vitamin A or retinol intake in lean NAFLD participants compared to lean controls without NAFLD ($p < 0.0001$ for vitamin A and $p = 0.017$ for retinol)^{10,44}. This suggests a potential association between low vitamin A intake and NAFLD risk in lean individuals. However, this association was not supported by other studies that reported no difference in vitamin A or β -carotene intake between the two groups^{10,70}.

Three studies explored the association between magnesium intake and NAFLD^{10,18,70}. A prospective study based in the United States observed a significant inverse relationship between magnesium intake from diet and lean NAFLD risk ($OR = 0.34$)¹⁸. However, this finding was not well supported by studies that compared magnesium intake between lean NAFLD and lean controls as one study observed lean NAFLD participants had higher magnesium intake while the second study observed no difference between the groups^{10,70}.

One prospective study based in China observed increasing choline intake was inversely associated with NAFLD risk ($OR = 0.68$ for females and 0.75 for males). Although this association was attenuated after adjustment for BMI and metabolic diseases ($OR = 0.88$ for females, $OR = 0.85$ for males), an analysis that stratified data by BMI identified a significant inverse association between increased choline intake and NAFLD risk in normal weight females

(OR = 0.72), but not in overweight or obese females (OR = 1.05). There was no association between choline intake and NAFLD risk for males in any weight category⁸¹.

Finally, multiple studies utilized comparisons between lean NAFLD and lean control groups to assess vitamins and minerals not previously discussed and lean NAFLD risk. All studies observed no difference in intake of copper, iodine, selenium, calcium, vitamin C, vitamin D, vitamin K, Vitamin E, and all B vitamins between the two groups^{10,44,63,64,66,70}. This suggests that these micronutrients may not be associated with the development of NAFLD in lean participants. One study reported lean NAFLD participants had significantly higher phosphorus and manganese intake compared to lean controls⁷⁰.

Other Nutrients

Finally, a total of eight studies examined topics related to the association between dietary fiber and/or cholesterol intake and lean NAFLD^{10,31,44,48,64-66,70}. Seven studies observed no significant association between dietary fiber intake and NAFLD risk. This included one study that reported no significant interaction between dietary fiber and a genetic trait known to influence NAFLD risk⁴⁸. Other studies observed no significant difference in dietary fiber intake between lean participants with NAFLD or NASH and lean participants without NAFLD or NASH^{10,31,44,48,64,66,70}. Five studies compared intake of cholesterol between lean NAFLD and other study groups. When comparing lean NAFLD to lean controls, three studies reported lean NAFLD participants had higher cholesterol intake ($p = 0.005$ to $p < 0.05$) and two study noted no difference in intake^{10,44,65,66,70}. Two studies observed lean NAFLD participants also had higher cholesterol intake than obese NAFLD participants ($p < 0.05$)^{66,70}. These findings overall suggest that high cholesterol intake is likely associated with increased NAFLD risk in lean participants.

Table 3.2. Risk and protective factors related to calorie intake and specific nutrients in lean NAFLD or fatty liver

Author	Study Design	Participant Characteristics	Weight Terminology	NAFLD diagnostic criteria	Main Findings
Agebratt et al ³² 2016 Sweden	Randomized uncontrolled trial 8 weeks duration	Total sample = 30 Categorized into fruit and nut intervention groups Mean age 24 years 60% male	Used non-obese, but no BMI or WC parameters provided as definition	MRI Hepatic fat monitored. Unclear if part of NAFLD diagnosis and no further diagnostic criteria specified. Participants excluded for (1) pre-existing medical conditions including HCV and HBV (2) use of thyroid medications. Alcohol intake not monitored	- Fruit group increased fructose intake ($p < 0.0001$), but no significant change in hepatic fat content at follow up - Nut group decreased fructose intake ($p = 0.007$) and increased in calorie intake ($p = 0.035$) and body weight ($p = 0.049$), but no significant change in hepatic fat content at follow up ($p = 0.99$)
Bo et al ⁴³ 2014 Italy	Prospective longitudinal 6 year follow up	Total sample = 1245 Data categorized by tertiles of calorie intake at dinner (T1-T3) Mean age 54-55 years 45.9% male	Non-obese used to categorize weight, but no BMI parameters provided as definition. Abdominal adiposity defined as WC ≥ 94 cm (male) and ≥ 80 cm (female)	NAFLD Liver Fat Score Liver fat score based on serum fasting insulin, fasting serum AST, AST/ALT ratio, and presence of MetS and/or T2DM. No other NAFLD diagnostic criteria specified. Alcohol intake not factored into diagnostic criteria	- In adjusted logistic regression, higher calorie intake at dinner positively associated with NAFLD incidence (comparing T3 to T1) OR = 1.56; 95% CI: 1.10–2.22; $p = 0.01$ - Dietary composition of dinner did not significantly differ despite calorie differences
Choi et al ⁴⁶ 2016 South Korea	Cross-sectional	Total sample = 100,177 Data categorized by quintiles of increasing sodium (Na) and potassium (K) intake (Q1-Q5) Mean age 37 years 46.5% male	Used term “low bodyweight”. Defined as BMI < 23 kg/m ² . No WC parameters provided Note: data on Na intake in men excluded due to anthropometric parameters exceeding inclusion criteria	Abdominal US NAFLD diagnostic criteria: Fatty liver indicated by US and the absence of (1) daily alcohol intake > 30 g (male) and > 20 g (female), (2) other causes of liver disease including HBV, HCV, (3) steatogenic medication use within the past year, (4) history of malignancy, CVD, HTN, and/or DM	Based on adjusted Poisson regression: - Na intake and Na:K ratio positively associated with NAFLD prevalence in females (Q5 vs Q1) Na PR = 1.32, 95% CI: 1.18–1.47, $P_{trend} < 0.001$ Na: K ratio PR = 1.13, 95% CI: 1.04–1.22, $P_{trend} < 0.001$ - Positive association between Na intake and NAFLD prevalence attenuated after adjustment for body fat (Q5 vs Q1) PR = 1.06, 95% CI: 0.95–1.17, $P_{trend} = 0.16$

					- K intake positively associated with NAFLD prevalence in males, but no association in females (Q5 vs Q1) Female PR = 0.97, 95% CI: 1.29- 0.16, $P_{\text{trend}} = 0.16$ Male PR = 1.12, 95% CI: 1.05-1.20, $P_{\text{trend}} < 0.001$ - Na intake positively associated with NAFLD prevalence when data stratified by BMI (Q5 vs Q1) PR (BMI < 23 kg/m²) = 1.28, 95% CI: 1.12–1.46, $P_{\text{trend}} < 0.001$ PR (BMI ≥ 23 kg/m²) = 1.14, 95% CI: 1.08–1.19, $P_{\text{trend}} < 0.001$
Duarte et al ³¹ 2018 Brazil	Cross-sectional	Total sample = 23 Data categorized into groups (1) lean NASH, (2) overweight NASH, (3), obese NASH, (4) lean controls, (5) obese controls Median age 30-53 years 52% male	Lean defined as BMI < 25 kg/m ² . No WC parameters provided.	Liver biopsy NASH diagnostic criteria: Liver histology and absence of (1) daily alcohol daily intake >30 g (males) and >20 g (females) (2) drug addiction (3) HBV or HCV, (4) schistosomiasis, (5) detectable serum autoantibodies associated with liver disease, (6) altered serum ceruloplasmin levels, and (7) hemochromatosis	No significant difference in calorie, carbohydrate, protein, fat, and dietary fiber intake between all study groups
Gonzalez-Granda et al ³⁶ 2018 Germany	Cross-over intervention study	Total sample = 12 Data categorized by diet (1) low fructose, (2) high fructose from natural sources, or (3) high fructose from fructose syrup diets Mean age 26-30 years 0% male	Lean defined as BMI = 20 to <25 kg/m ² . No WC parameters provided.	FLI, liver enzymes (GGT, AST, ALT), HRI Evaluated “fatty liver”. Unclear if considered NAFLD. No diagnostic criteria specified. Participants excluded for following reasons (1) smoking, (2) fructose malabsorption, (3)	No significant change in liver enzymes, FLI, and HRI during any of the diet phases

				pregnancy, (4) chronic GI diseases (5) GI surgery in the past (except appendectomy), (6) chronic anemia, (7) chronic hepatic or renal disease, (8) DM, (9) consuming illnesses including cancer or HIV, (10) use of drugs affecting lipid or glucose metabolism	
Honarvar et al ⁸⁴ 2017 Iran	Cross-sectional	Total sample = 478 Data categorized as lean non-NAFLD, lean NAFLD, non-lean non-NAFLD, and non-lean NAFLD Median age 42 years 40.6% male	Lean defined as BMI < 25 kg/m ² . No definition for WC provided.	Abdominal US NAFLD diagnostic criteria not specified. Participants excluded from study for following reasons (1) DM, (2) pregnancy or given birth in past 6 months, (3) alcohol consumer	- No significant difference in carbohydrate, protein, fat, SFA, MUFA, and PUFA intake when comparing all study groups In adjusted logistic regression (included all study groups, adjusted for BMI): - Total fat, total carbohydrate, and PUFA intake positively associated with NAFLD risk Fat OR = 1.023, 95% CI: 1.005-1.041, p = 0.014 Total carbohydrates OR = 1.99, 95% CI: 1.982-1.997, p = 0.004 PUFA OR = 1.06, 95% CI: 1.008 - 1.120, p = 0.02. - Positive association between PUFA intake and NAFLD risk most pronounced in lean NAFLD (data not provided) - No significant association between intake of protein, SFA, and MUFA's and NAFLD risk in all study groups
Kwak et al ¹⁰ 2018 South Korea	Cross-sectional	Total sample = 209 Data categorized into groups (1) non-obese NAFLD, (2) non-obese controls, (3) obese NAFLD, (4) obese controls Age 39-41 years	Non-obese and normal weight used interchangeably. Defined as BMI < 25 kg/m ² . No WC parameters provided	Abdominal CT scan NAFLD diagnostic criteria: Fatty liver on CT scan and absence of daily alcohol intake > 30 g (males) or > 20 g (females) in past two years	Lean NAFLD vs lean controls: Higher carbohydrate intake (p = 0.011) and lower retinol intake (p = 0.017) No significant difference in total calorie, fat, vegetable fat, animal fat, protein, dietary fiber, vitamin A, β-carotene, vitamin D, vitamin E, vitamin K, vitamin C, all B vitamins, calcium, sodium,

		No data on sex distribution provided		Participants excluded from study for (1) steatogenic medications use in past month (including herbal and prescription medicines), and/or (2) HBV, HCV, or autoimmune hepatitis	potassium, magnesium, cholesterol, SFA, MUFA, and PUFA intake - No data provided comparing non-obese to obese controls and obese NAFLD - In lean participants, NAFLD prevalence increased as carbohydrate intake increased ($P_{\text{trend}} = 0.023$, no other data provided) - In fully adjusted logistic regression, carbohydrate energy ratio (% of kcal) independent predictor of NAFLD Exp (B) = 1.181, 95% CI: 1.025-1.362, $p = 0.022$
Kwon et al ⁵⁰ 2012 South Korea	Cross-sectional	Total sample = 14913 Data categorized by percentage (%) of calories from carbohydrates or fats. Carbohydrate % range < 60% to > 75%, fat % range < 10% to 50-60% Mean age 44 years 42.2% male	No specific terminology or BMI or WC parameters provided to classify weight	Liver enzymes (AST and ALT) Unclear if evaluating fatty liver or NAFLD risk. No NAFLD diagnostic criteria provided Participants excluded from study for (1) weekly alcohol intake > 140 g (males) or > 70 g (females), (2) HBV or HCV infection, (3) liver cirrhosis, (4) hepatocellular carcinoma	- Pearson correlation coefficients showed carbohydrate % positively associated with ALT and AST (0.023 and 0.059), fat % negatively associated (-0.044 and -0.080) - In fully adjusted logistic regression, ALT and AST positively associated with increasing carbohydrate % OR = 1.008, 95% CI: 1.003-1.013, $p = 0.001$ - Comparing abnormal AST and ALT to carbohydrate % formed J-shaped graph, lowest point at 50-60% of kcal from carbohydrates - Comparing abnormal AST and ALT and fat % formed U-shaped graph, lowest point 30-40% of kcal from fat - Highest frequency of abnormal AST and ALT observed with 35-45% of kcal from carbohydrates

Li et al ⁷⁰ 2019 China	Matched case-control study	Total sample = 351 Data categorized by lean controls, lean NAFLD, obese controls, obese NAFLD Mean age 43-45 years 49% male	Lean and non-obese used interchangeably. Defined as BMI < 24 kg/m ² . Parameters for WC not provided	Abdominal US NAFLD diagnostic criteria: Abnormal US images indicating fatty liver without the following (1) alcohol intake >140 g/week (male) and >70 g/week (female), (2) infection with HBV, HCV, or dual HBV/HCV, (3) hepatolenticular degeneration, autoimmune diseases, (5) total parenteral nutrition within past 4 months, (6) hepatotoxic drugs intake, (7) malignancies, (8) DM or (9) pregnancy	Lean NAFLD vs obese NAFLD: - Lower total carbohydrate, zinc, and copper intake (p < 0.05) - No difference in total calorie, protein, fat, cholesterol, fiber, calcium, phosphorus, potassium, sodium, magnesium, manganese, iron, selenium, iodine, salt, vitamin A, vitamin C, vitamin E, thiamine, riboflavin, vitamin B6, folate, and niacin intake Lean NAFLD vs lean controls: - Higher total calorie, carbohydrate, protein, fat, cholesterol, fiber, phosphorus, potassium, magnesium, iron, and manganese intake (p < 0.05) - No difference in calcium, sodium, salt, zinc, selenium, copper, iodine, vitamin A, vitamin C, vitamin E, thiamine, riboflavin, vitamin B6, folate, and niacin intake
Lu et al ¹⁸ 2022 USA	Prospective cohort study 30 year study with follow up at year 7, 20, and/or 25	Total sample = 2,685 Data categorized by quintiles of Magnesium (Mg) intake (Q1-Q5) Mean age 50 years 41.9% male	Normal weight used to classify weight but no BMI or WC parameters provided as definition	Non-contrast CT scan at 25 year follow up NAFLD diagnostic criteria not specified. Participants excluded from study if the following were present during follow up (1) pregnancy, (2) self-reported liver disease (3) alcohol intake ≥ 14 drinks/week (males) or ≥ 7 drinks/week (females), (4) hepatotoxic medication use, or (5) HIV	- In multivariate adjusted model, total Mg intake (diet + supplements) inversely associated with NAFLD risk (Q5 vs. Q1) OR 0.45, 95% CI 0.23-0.85, P_{trend} = 0.03 - Inverse relationship remained after removal of Mg supplement users (Q5 vs. Q1) OR 0.34, 95% CI 0.14, 0.82, P_{trend} = 0.04
Musso et al ⁴⁴ 2007 Italy	Cross-sectional	Total sample = 138 Data categorized into Insulin Sensitive (IS) NAFLD and Insulin	Used term non-obese. Defined as BMI < 30 kg/m ² (males) or < 28 kg/m ² (females). Abdominal obesity defined as WC > 102	Abdominal US NAFLD diagnostic criteria included (1) elevated ALT and AST ≥ 6 months, (2) US confirmed fatty liver, (3)	- IS NAFLD had lower vitamin A intake compared to IS controls (p < 0.0001) - No difference between two groups for intake of calories, fat, carbohydrates, simple

		Sensitive (IS) control groups Mean age 48-52 years 73.4% male	cm (males) and > 88 cm (females)	daily alcohol intake < 20 g (males) and < 10g (females), and (4) no other causes of liver or biliary tract disease (i.e., viral hepatitis, autoimmune disorders, CD, abnormal copper metabolism, α 1-antitripsin deficiency, hemochromatosis, abnormal thyroid function, occupational hepatotoxins exposure, use of steatogenic medications or those affecting glucose or lipid metabolism)	carbohydrates, protein, cholesterol, fiber, SFA, MUFA, PUFA, and PUFA: SFA ratio, vitamin C, and Vitamin E
Nier et al ³⁷ 2019 Germany	Cross-over intervention study	Total sample = 12 Mean age 26 years 41.7% male	Normal weight used to classify weight, No BMI or WC parameters provided for definition	ALT and AST Evaluated “liver health”. Relationship to NAFLD unclear. Participants excluded from study for (1) DM, (2) HBP, (3) liver diseases, (4) smoking, or (5) daily alcohol intake > 20 g (male) or >10 g (female)	Compared to levels during standardization diet: - ALT increased after fructose-enriched diet ($p < 0.05$) but did not significantly change after glucose-enriched diet. - AST did not significantly change after fructose or glucose-enriched diets
Oya et al ⁶² 2010 Japan	Cross-sectional	Total sample = 792 Data categorized by sex and tertiles of increasing intake of select dietary fats (T1-T3) Mean age 51-52 years 37.4% male	Non-obese used to categorize weight but no BMI or WC parameters provided as definition NOTE: female data not reported due to not meeting anthropometric inclusion criterion	Abdominal US NAFLD diagnostic criteria: Fatty liver identified on US and participant’s estimated alcohol intake < 0 g/day Participants excluded from study for (1) DM, (2) CVD, (3) HBV or HCV, (4) HTN or dyslipidemia treated with medication	- Multivariate adjusted logistic regression identified linear negative correlation between EPA and EPA + DHA intake and NAFLD risk (T3 vs T1) EPA OR = 0.45, 95% CI: 0.23-0.90, $P_{trend} = 0.024$ EPA + DHA OR = 0.48, 95% CI: 0.24-9.95, $P_{trend} = 0.035$ - No significant association between n-3 PUFA or DHA intake and NAFLD risk

Park and Kang ⁴⁸ 2020 South Korea	Cross-sectional	Total sample = 27,374 Data categorized into groups with or without presence of genetic trait associated with NAFLD risk (minor allele haplotype 22q13 loci) Mean age 54-55 years 35.9% male	Lean defined as BMI < 25 kg/m ² . Abdominal obesity defined as WC > 90 cm (males) and > 85 cm (females)	Abdominal US NAFLD diagnostic criteria: Fatty liver confirmed on US without alcohol intake >40 g/d (males) and >30 g/d (females) Participants excluded from study if “serious disease present”	- Participants with minor allele haplotype 22q13 loci and consumed high carbohydrate diet (> 75% of kcal) had higher NAFLD incidence compared to those with trait and consuming low carbohydrate diet (p < 0.001) - No significant interaction between minor allele haplotype 22q13 loci and total calories, protein, fat, and fiber intake
Sepulveda et al ³⁰ 2019 Mexico	Cross-sectional	Total sample = 505 Participants identified with risk for NASH categorized by body weight: normal weight (NW), overweight (OW), obese class I-II (OB I-II), and obese class III (OB III) Mean age 40 years 32% male	Normal weight defined as BMI = 18.5-24.9 kg/m ² . No WC parameters provided.	Liver biopsy or Transient Elastography (TE) Risk for NASH based on presence of at least one of the following: elevated FPG, TG, HOMA-IR, AST, and/or ALT. Liver biopsy or TE used to evaluate liver stiffness or fibrosis Participants excluded from study for the following (1) daily alcoholic intake > 40 g (males) or >20 g (females), (2) acute or chronic HBV or HCV (3) other causes of liver disease including autoimmune liver disease, hemochromatosis, Wilson’s disease, α -1 antitrypsin deficiency, primary sclerosing cholangitis, primary biliary cholestasis, drug-induced hepatotoxicity	- NW group had higher total fat (% of kcal) compared to OW, OB I-II, and OB III groups (42% vs 27.8-31.3%, p = 0.009) - OB III group with higher total calorie intake compared to other groups - No difference in % of kcal from protein, carbohydrates, SFA, MUFA, PUFA among all groups
Shen et al ⁸⁰ 2019 China	Prospective study 8 years of follow up	Total sample = 35,023 Data categorized by perceived salt intake: low (< 6 g/day), medium (6-9 g/day), or high ($\geq$ 10 g/day)	No specific terminology or BMI or WC parameters provided to classify weight. Groups categorized into BMI < 25 or $\geq$ 25 kg/m ² in stratified analysis	Abdominal US NAFLD diagnostic criteria: (1) Fatty liver on US, (2) normal or abnormal serum transaminases, (3) no alcohol consumption prior to the study, at baseline, or	In fully adjusted Cox proportional hazard regression, high salt intake positively associated with NAFLD risk (comparing high to low intake) HR = 1.19, 95% CI: 1.02-1.39, P_{trend} = 0.03

		Mean age 50-52 years 64.6% male		during follow-up (based on self-report)	Positive association between higher salt intake and NAFLD risk persisted in subgroup analysis, especially in females and BMI < 25 kg/m² Approximate HR = 1.20 (BMI < 25) and 1.30 (females), $P_{\text{trend}} < 0.05$
Suomela et al ³⁴ 2015 Finland	Prospective Follow up 3-15 years	Total sample = 1,998 Data categorized into groups: normal weight/normal liver, normal weight/fatty liver, overweight/normal liver, overweight/fatty liver Mean age 42-43 years 45.5% male	Normal weight defined as BMI < 25 kg/m ² . No WC parameters provided	Abdominal US Evaluated hepatic steatosis. Unclear if part of NAFLD diagnostic criteria specified Did not exclude participants from study for other secondary causes of fatty liver including (1) medicinal, (2) viral infections, or (3) autoimmune liver diseases	- Normal weight with fatty liver group with lower protein (% kcal) compared to overweight groups with or without fatty liver ($p = 0.01$ and $p < 0.05$ respectively) - All groups significantly differed in carbohydrate intake ($p = 0.0002$) but unclear how normal weight/fatty liver group specifically differed from other study groups
Tabuchi et al ⁶³ 2010 Japan	Cross-sectional, case control	Total sample = 77 Data categorized into lean control and NAFLD groups Mean age 51-52 years 100% male	Non-obese defined as BMI < 25 kg/m ² . Abdominal adiposity defined as WC ≥ 85 cm	Abdominal US NAFLD diagnostic criteria: Fatty liver on US and absence of (2) daily alcohol intake < 20 g, (3) autoimmune liver diseases, HCV, HBV, (4) history of excess alcohol intake, (5) history of hepatotoxic medication use Participants were excluded from the study if had DM or hypothyroidism	- No difference between groups for total calorie, protein, carbohydrate, fat, vitamin C, vitamin E, iron, zinc, SFA, MUFA, PUFA, n-6 PUFA, or n-3 PUFA intake - Partial correlation coefficient showed SFA intake positively correlated with M30 antigen (NAFLD biomarker) in NAFLD group (0.379, $p = 0.03$) - No association between SFA intake and NAFLD risk in multivariate adjusted logistic regression
Tajima et al ⁵⁹ 2017 Japan	Cross-sectional	Total sample = 2444 Data categorized by quartiles of rice, noodle, and bread intake (Q1-Q4)	No terminology or BMI and WC parameters provided to categorize weight	Abdominal US NAFLD diagnosis based on assumption that fatty liver was related to NAFLD due to participants being excluded from study for (1)	In fully adjusted logistic regression: Carbohydrate intake positively associated with NAFLD prevalence in females (Q4 vs Q1) OR = 2.22, 95% CI: 1.16, 4.27, $P_{\text{trend}} = 0.008$

		Mean age 52-53 years 40% male		alcohol intake ≥ 30 g/d (male) and ≥ 20 g/d (females), (2) self-reported possibility of pregnancy, (3) other self-reported liver diseases, (4) positive or unknown hepatitis B or C serology, (5) history of gastrectomy, (6) use of medication for HLD or DM, (7) use of breast cancer medications, (8) use of hormone replacement therapy, (9) T2DM	No significant association between carbohydrate intake and NAFLD prevalence in males (Q4 vs Q1) OR = 1.57, 95% CI: 0.93-2.63, $P_{\text{trend}} = 0.11$
Toshimitsu et al ⁶⁴ 2007 Japan	Cross-sectional	Total sample = 46 Categorized into groups (1) NASH, (2) simple fatty liver (FL), (3) healthy controls. Groups further categorized into age ranges (20-39 years, 40-59 years, ≥ 60 years) Mean age 43-51 years 63% male	No terminology, BMI, or WC parameters provided to classify weight	Liver biopsy NAFLD/NASH diagnostic criteria not specified though secondary causes of liver disease ruled out during initial data collection including (1) daily alcohol intake > 30 g (males) and > 20 g (females), (2) hepatotoxic drug use, (3) HBV or HCV infection, (4) genetic metabolic diseases, (5) autoimmune liver diseases, (6) biliary diseases, (7) thyroid diseases	- Compared to FL group ages 20-59 years, NASH group with higher total carb intake (% of kcal) and lower intake of zinc ($p < 0.05$ for all) - Compared to FL group ages 40-59 years, NASH group with lower protein intake (% of kcal) ($p < 0.05$) - No significant difference in fat, simple carbs, SFA, MUFA, PUFA, PUFA/SFA ratio, omega-6/omega-3 ratio, vitamin C, vitamin E, iron, or copper or fiber intake between all study groups and age ranges - In logistic regression, NASH associated with high carbohydrate intake and low protein, PUFA, PUFA/SFA ratio, and zinc intake (comparison group and CI not specified) Carbs OR = 1.005, $p = 0.274$ Protein OR = 0.959, $p = 0.179$ PUFA OR = 0.971, $p = 0.769$ PUFA/SFA ratio OR = 2.951, $p = 0.321$ Zinc OR = 0.842, $p = 0.224$

Yamamoto et al ⁶⁵ 2023 Japan	Cross-sectional	Total sample = 464 Data categorized into groups non-NAFLD and NAFLD group. Further categorized into groups with APOC3 T-455C genotypes (TT, TC, and CC) Mean age 62 years 37.1% male	Non-obese defined as BMI < 25 kg/m ² . No WC parameters provided	Abdominal US No NAFLD diagnostic criteria specified besides US confirmed fatty liver. Participants excluded from study for (1) history or treatment of hepatitis, (2) daily alcohol intake >30 g (males) or >20 g (females)	- In participants with APOC3 genotypes, NAFLD interacted with total fat intake (p = 0.006), vegetable fat (p = 0.017), MUFAs (p = 0.002), PUFAs (p = 0.015), cholesterol (p = 0.031), n-3 fatty acids (p 0.038), and n-6 fatty acids (p = 0.025) - Those with TT genotype and NAFLD with significantly lower carbohydrate intake (p = 0.049) and higher total fat (p = 0.001), vegetable fat (p = 0.002), SFA (p = 0.020), MUFAs (p < 0.001), PUFAs (p = 0.008), cholesterol (p = 0.005), and n-6 fatty acids (p = 0.008) intake compared to those with TT genotype without NAFLD - No association between other genotypes and all dietary factors
Yasutake et al ⁶⁶ 2009 Japan	Cross-sectional	Total sample = 56 Data categorized by groups: non-obese controls, non-obese NAFLD, and obese NAFLD Mean age 47-54 years 46.4% male	Non-obese participants defined as BMI < 25 kg/m ² . No WC parameters provided	Abdominal US, liver biopsy, or CT scan NAFLD diagnostic criteria not specified. Participants excluded from study for hyperglycemia and/or hypertriglyceridemia	Obese NAFLD vs nonobese NAFLD: - Higher intake of calories (p = 0.0397), carbohydrates (p = 0.0456), PUFA (p = 0.0195 and lower cholesterol (p = 0.0378) - No difference in protein, fat, MUFA, or SFA Non-obese NAFLD vs nonobese controls: - Higher intake of cholesterol and PUFA (p < 0.05) - No difference in calories, carbohydrate, protein, fat, SFA, or MUFA intake No significant difference in iron, zinc, β-carotene, vitamin E and C, and dietary fiber intake between all groups
Yu et al ⁸¹ 2014 China	Prospective study Follow up every 2-3 years	Total sample = 56,195 Data categorized by sex and quintiles of increasing choline intake (Q1-Q5)	Normal weight defined as BMI < 25 kg/m ² . No WC parameters provided	Self-reported by participants by providing proof of NAFLD diagnosed by physician using abdominal US	In multivariate adjusted model, choline intake inversely associated with NAFLD risk (Q5 vs Q1) Females OR = 0.68, 95% CI: 0.59-0.79, P_{trend} = 0.0001 Males OR = 0.75 95% CI: 0.60-0.93, P_{trend} = 0.004

Mean age 50-54 years 33.4% male	NAFLD diagnostic criteria: US confirmed fatty liver and alcohol intake $\leq$ 28 g/d (males) or $\leq$ 14 g/d (females) at baseline Participants excluded from study if reported hepatitis, CVD, or cancer at baseline	• Adjustment for BMI and metabolic diseases attenuated association (Q5 vs Q1) Females OR = 0.88, 95% CI: 0.75- 1.03, $P_{\text{trend}} = 0.05$ Males OR = 0.85, 95% CI: 0.68 -1.06, $P_{\text{trend}} = 0.09$ • Stratified analysis indicated association between choline intake and NAFLD risk in normal weight females, but not overweight or obese females OR (BMI < 25) =0.72, 95% CI: 0.57-0.91, $P_{\text{trend}} = 0.007$ OR (BMI $\geq$ 25) = 1.05, 95% CI: 0.84-1.31, $P_{\text{trend}} = 0.99$ • No association between choline intake and NAFLD risk in any weight category in males • No association between protein, SFA, MUFA, and PUFA intake and NAFLD risk (data and statistical analysis not provided)
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3.6 Beverage Intake and Lean NAFLD

A total of 22 articles examined the relationship between intake of different beverages and lean NAFLD risk. Most studies focused on alcohol (n = 16), while four studies focused on soda consumption and three studies examined other beverages including coffee and tea. Detailed data are shown in Table 3.3.

Alcohol Intake

Among the sixteen studies evaluating alcohol intake in lean NAFLD populations, there was significant heterogeneity in study design, alcohol intake levels evaluated, and results^{20,33–35,44,48,52,55–58,65,67,68,70,81}. Depending on the alcohol level evaluated, results indicated that alcohol intake had no association, a positive association, or a negative association with NAFLD or fatty liver risk in lean populations.

Six studies indicated that alcohol intake was not a predictor of fatty liver risk in lean population. This included one prospective and five cross-sectional studies conducted in Japan, China, South Korea, or Italy^{44,48,56,65,70,81}. Most studies examined populations with low alcohol intake due to strict exclusion criteria and alcohol intake ranged from as little as 3–6 grams/day to 40 grams of alcohol/day^{44,48,65,70,81}. Two studies reported no significant interaction between genetic traits known to influence NAFLD risk and alcohol intake (exclusion criteria restricted daily alcohol intake to < 20–30 g in females and < 30–40 g in males)^{48,65}. Three studies that compared alcohol intake between lean participants with or without NAFLD were observed to have no significant difference in alcohol intake (average intake ranged from 3–8 g/day)^{44,65,70}. One of these studies also reported no significant difference in alcohol intake between lean NAFLD and obese controls and obese NAFLD participants⁷⁰. Interestingly, one study did evaluate higher alcohol intake and while researchers reported a higher fatty liver prevalence in

those consuming alcohol ≥ 60 g/day compared to those consuming < 60 g/day ($p < 0.0001$), an odds ratio analysis indicated habitual alcohol intake was not an independent predictor of fatty liver when analyzing data from the beginning and end of the 12 year study⁵⁶.

Seven studies observed alcohol intake was positively associated with NAFLD or fatty liver risk. These studies included five cross-sectional and three prospective study conducted in South Korea, Japan, or Finland^{33–35,52,55–57}. The amount of alcohol associated with increased NAFLD risk varied in the studies ranging from as little as 1–40 g/day to over 100 g/day. Three studies reported low amounts of alcohol were positively associated with NAFLD or fatty liver risk in lean participants, which was defined as daily intake 1–40 g, < 20 g, or 10–20g in females and 10–30 g in males depending on the study (HR = 1.06, OR = 1.29–1.61)^{34,35,52}. One of these studies was a large prospective study ($n = 190,048$) and noted that low levels of alcohol intake was positively associated with NAFLD risk in lean participants and inversely associated with NAFLD in obese participants (HR = 1.06 in lean group versus 0.74 in obese group)⁵². Another study reported a more pronounced positive association between alcohol intake < 20 g/day and fatty liver in lean participants compared to overweight participants (OR = 1.47 in lean group versus 1.20 in overweight group)³⁴. When considering higher levels of alcohol intake, two studies reported moderate alcohol intake (defined as daily intake 41–60 g or 30–60 g) to be positively associated with fatty liver risk, four studies reported high (defined as daily intake of > 20 g, > 50 g, 60–90 g, or 61–100 g), and very high alcohol intake (defined as daily intake > 90 g, or > 100 g) were positively associated with NAFLD or fatty liver risk in lean participants. The ORs for moderate alcohol intake were 2.416–3.77, high alcohol intake were 1.286–4.724, and very high alcohol intake were 4.724–6.73^{34,35,55,57}. Additionally, two studies using group comparisons identified trends suggestive of a positive association between alcohol intake and

fatty liver risk. One study reported significantly higher fatty liver prevalence in those consuming alcohol ≥ 60 g/day compared to those consuming < 60 g/day (about 27% versus 21%, $p < 0.0001$) and another study reported significantly higher alcohol intake in individuals with fatty liver compared to those without fatty liver (116 g/week versus 55 g/week, $p < 0.001$)^{33,56}. Of note, some differences were observed in the association between moderate to very high alcohol intake and NAFLD risk when comparing lean participants to overweight or obese participants. While one study reported heavy drinking to be positively associated with fatty liver risk in lean participants, it was negatively associated with fatty liver in obese participants (OR = 1.286–2.216 in lean participants versus 0.618–0.765 in obese participants)⁵⁷. Another study observed that the positive association between high alcohol intake and fatty liver was more pronounced in lean participants compared to overweight participants (OR = 3.08 in lean group versus 1.72 in overweight group)³⁴.

Five studies reported potential inverse association or protective effect of alcohol intake on NAFLD or fatty liver in lean individuals. All studies were cross-sectional and based in Japan^{20,57,58,67,68}. Interestingly, one study reported that all levels of alcohol intake (categorized as < 30 g/day, 30–60 g/day, and ≥ 60 g/day) were inversely associated with fatty liver when compared to no alcohol intake (ORs corresponding with increasing alcohol intake = 0.682, 0.771, and 0.840). When comparing levels of alcohol intake to fatty liver prevalence, there was a significantly higher prevalence of fatty liver in nondrinkers compared to light, moderate, and heavy drinkers (47.7% prevalence rate in non-drinkers versus 38.1–42% in alcohol consumers, $p < 0.001$). A U-shaped graph also indicated lowest fatty liver prevalence rates were associated with 30-60 grams alcohol daily, suggesting that moderate alcohol intake was the most protective against fatty liver⁶⁷. Another study reported similar findings where all levels of alcohol intake

ranging from 0.5% to 15% of calories were inversely associated with fatty liver prevalence (PRs for increasing alcohol intake = 0.87, 0.73, 0.72, and 0.77), but a non-linear trend indicated moderate alcohol intake (defined as approximately 7% of calories) was associated with lowest fatty liver prevalence (PR = 0.72). However, these results were attenuated and no longer significant after adjusting the model for BMI (PRs for increasing alcohol intake = 1.04, 0.94, 0.87, 0.92, $P_{\text{trend}} = 0.06$)⁵⁸. The remaining studies reported moderate alcohol intake (defined as daily intake < 20 g, 23 g, or 20-50 g) was inversely associated with NAFLD or fatty liver risk in lean individuals while noting some differences between biological sexes and BMI categories (ORs = 0.393–0.66)^{20,57,68}. For example, one study reported daily alcohol intake of 20-50 grams was inversely associated with fatty liver in females (OR = 0.393), but was positively associated with fatty liver in males (data not provided)⁵⁷. Another study reported heavy drinking (defined as 46 to > 69 g alcohol daily) was inversely associated with fatty liver risk in males (OR = 0.57) and females (OR = 0.85), but the association was not significant in females⁶⁸. Finally, a third study reported daily alcohol intake < 20 grams was inversely associated with NAFLD in females with BMI < 25 kg/m² (OR = 0.66), but not in females with BMI < 22 kg/m² or males in either BMI category (data not provided)²⁰.

Soda Intake

Four studies evaluated the association between soda intake and NAFLD risk^{59,82,84,85}. A large cross-sectional study in China observed a significant positive association between more frequent soda intake and NAFLD among individuals with normal and elevated ALT (OR = 1.26 and 1.32 respectively)⁸². In contrast, two smaller cross-sectional studies based in Iran and Japan found no association between soft drink intake and NAFLD prevalence in lean participants^{59,84}. A prospective study based in India comparing soda intake between groups and observed lean

NAFLD participants had significantly lower soft drink consumption than obese NAFLD participants (17 ± 7.5 versus 12 ± 1.7 soft drinks/month, $p = 0.005$)⁸⁵.

Other beverages

Three articles examined the influence of other beverages including coffee and tea intake on risk of NAFLD or fatty liver^{48,51,54}. A cross-sectional study reported no significant interaction between coffee or tea intake and genetic traits associated with NAFLD risk found that both low and high intake of coffee intake (defined as < 7.5 g coffee/day or > 7.5 g coffee/day) did not interact with NAFLD risk in this population ($P_{\text{interaction}} > 0.05$ for all)⁴⁸. In contrast, two other studies found associations between coffee intake and fatty liver risk^{51,54}. One study reported coffee intake > 3 cups/day was inversely associated with fatty liver risk when compared to non-drinkers (OR = 0.59). Another large retrospective longitudinal study reported that no amount of coffee intake (ranging from none to ≥ 5 cups/day) was associated with fatty liver risk at baseline. However, increased coffee intake over time was associated with lower fatty liver risk compared to no change in coffee intake over time (HR = 0.96). Decreased coffee intake was not associated with lower fatty liver risk (HR = 0.99)⁵¹. Two studies studying tea intake reported no association between tea and NAFLD or fatty liver risk^{48,54}.

Table 3.3 Risk and protective factors related to beverage intake in lean NAFLD or fatty liver

Author	Study Design	Participant Characteristics	Weight Terminology	NAFLD diagnostic criteria	Main Findings
Akahane et al ⁶⁷ 2020 Japan	Cross-sectional	Total sample = 2429 Data categorized by alcohol intake frequency: non-drinkers (ND, 0 g/day), light drinkers (LD, < 30 g/day), moderate drinkers (MD, 30-60 g/day), heavy drinkers (HD, ≥ 60 g/day) Mean age 53-54 years 100% male	Normal weight defined as BMI < 23 kg/m ² . Abdominal adiposity defined as WC ≥ 85 cm	Abdominal US Evaluated fatty liver. Relationship to NAFLD unclear. No diagnostic criteria specified. Participants excluded from the study if positive for HBV or HCV infection.	- In adjusted multivariate logistic regression, all alcohol intake levels inversely associated with fatty liver (compared to non-drinkers) ND OR = 1.00 LD OR = 0.682, 95% CI: 0.549–0.846, p = 0.001 MD OR = 0.771, 95% CI: 0.675–0.880, p < 0.001 HD OR = 0.840, 95% CI: 0.749–0.941, p = 0.003 - Inverse association remained for all types of alcoholic beverages - GGT and AST significantly increased as alcohol intake increase (p < 0.001 for both), but U-shaped graph indicated lowest ALT levels associated with MD (p = 0.011) - U-shaped graph indicated MD associated with lowest fatty liver prevalence and ND associated with highest fatty liver prevalence (ND prevalence = 47.7% vs MD prevalence = 38.1%, p < 0.001)
Chang et al ⁵² 2020 South Korea	Prospective Median follow up 4.1 years	Total sample = 190,048 Data categorized into non-drinkers (0 g/day all sexes), light drinkers (1 to < 10 g/day all sexes), moderate drinkers (10 to < 20 g/day for females or 10 to < 30 g/day for males) Mean age 35-37 years 44.2% male	Non-obese defined as BMI ≤ 25 kg/m ² . No WC parameters provided.	Abdominal US No NAFLD diagnostic criteria provided. Participants excluded for the following: (1) history of malignancy, (2) history of liver cirrhosis or fibrosis, (3) daily alcohol intake > 30 g (males) or > 20 g (females), (4) HBV or HCV infection, (5) known liver disease or use of medications for liver disease, (6) steatogenic drug use within past year	In fully adjusted parametric proportional hazard model: - Moderate drinking positively associated with NAFLD in non-obese (moderate vs non-drinking) HR = 1.06, 95% CI: 1.03-1.10, P_{trend} < 0.001 - Moderate alcohol intake inversely associated with NAFLD in obese (moderate vs non-drinking) HR = 0.74 (0.70-0.77), P_{trend} < 0.001

Chung et al ⁵¹ 2020 South Korea	Retrospective longitudinal study Mean time period between baseline and follow up was 2.8 years	Total sample = 91,436 Data categorized by coffee consumption: none, < 1 cup/day, 1-2 cups/day, 3-4 cups/day, ≥ 5 cups/day Mean age 37 years 49.58% male	No terminology, BMI, or WC parameters specified to classify weight	Abdominal US Evaluated fatty liver disease. Relationship to NAFLD unclear. No diagnostic criteria specified. Participants excluded from study for (1) taking medications for DM, HTN, or HLD treatment, (2) secondary causes of fatty liver including HBV, HCV, or cancer	- No significant association between any amount of coffee consumption and fatty liver incidence at baseline - Increased coffee intake between baseline and follow up associated with lower fatty liver risk (increased intake vs no change) HR = 0.96, 95% CI: 0.91-0.99 - Decreased coffee intake between baseline and follow up not associated with lower fatty liver risk (decreased intake vs no change) HR = 0.99, 95% CI: 0.95-1.03 - Same trends occurred in males, but not females when results stratified by sex
Honarvar et al ⁸⁴ 2017 Iran	Cross-sectional	Total sample = 478 Data categorized as lean non-NAFLD, lean NAFLD, non-lean non-NAFLD, and non-lean NAFLD Median age 42 years 40.6% male	Lean defined as BMI < 25 kg/m ² . No definition for WC provided.	Abdominal US NAFLD diagnostic criteria not specified. Participants excluded from study for following reasons (1) DM, (2) pregnancy or given birth in past 6 months, (3) alcohol consumer	In fully adjusted model, no significant association between intake of soft drinks and NAFLD risk OR = 1.00, 95% CI: 0.99 - 1.00, p = 0.99 Note: analysis combined all study groups, adjusted for BMI
Imatoh et al ⁵⁴ 2015 Japan	Cross-sectional	Total sample = 1059 Data categorized into non-HS and HS groups. Further categorized by coffee or tea intake (none, 1-2 cups/day, ≥ 3 cups/day) Mean age 48-49 years 100% male	No terminology, BMI, or WC parameters specified to classify weight	Abdominal US Evaluated HS. Relationship to NAFLD unclear. No diagnostic criteria provided Participants excluded from study if positive for HBV or HCV	- In adjusted logistic regression, coffee intake > 3 cups/day associated with lower OR for HS compared to non-drinkers OR = 0.59, 95% CI: 0.38-0.90, P_{trend} < 0.05 - No significant association between HS risk and green tea intake.
Iwata et al ⁵⁵ 2013 Japan	Cross-sectional	Total sample = 1809 Mean age 35 years 100% male	No terminology, BMI, or WC parameters provided to classify weight	Liver enzymes (AST, ALT, GGT) Evaluated "hepatocellular injury". No NAFLD diagnosis specified.	Fully adjusted multivariate logistic regression indicated: Alcohol intake > 90 g/day positively associated with elevated ALT compared to lower intake levels OR = 1.788, 95% CI: 1.025-3.121

				Participants excluded from study for history of (1) stroke, (2) ischemic heart disease, (3) chronic renal failure, (4) alcohol dependency diagnosed by psychiatrist (5) liver cirrhosis or cancer (6) HBV or HCV	Alcohol intake > 30 g/day positively associated with elevated AST OR (30-60 g/day) = 2.416, 95% CI: 1.578-3.698 OR (60-90 g/day) = 2.189, 95% CI: 1.157-4.141 OR (>90 g/day) = 4.724, 95% CI: 2.671-8.354
Kojima et al ⁵⁶ 2003 Japan	Repeated cross-sectional	Total sample = 113,721 Data categorized as first-time examinees and repeaters. Further categorized as non-drinkers or habitual drinkers (≥ 60 g/day) Mean age 46 years 41.2% male	Non-obese defined as BMI < 25 kg/m ² . No WC parameters provided	Abdominal US Evaluated fatty liver. Relationship to NAFLD unclear. No NAFLD diagnostic criteria specified Participant exclusion criteria not specified	- In analysis of first-time examinees, alcohol intake > 60 g/day associated with higher fatty liver prevalence compared to non-drinkers. (about 27% vs 20%, $p < 0.0001$) - Alcohol not independently associated with fatty liver incidence based on multivariate analysis of (1) fatty liver risk factors in first time examinees and (2) a comparison of data from first and last 3 years of study
Li et al ⁷⁰ 2019 China	Matched case-control study	Total sample = 351 Data categorized by lean controls, lean NAFLD, obese controls, obese NAFLD Mean age 43-45 years 49% male	Lean and non-obese used interchangeably. Defined as BMI < 24 kg/m ² . Parameters for WC not provided	Abdominal US NAFLD diagnostic criteria: Abnormal US images indicating fatty liver without the following (1) alcohol intake >140 g/week (male) and >70 g/week (female), (2) infection with HBV, HCV, or dual HBV/HCV, (3) hepatolenticular degeneration, autoimmune diseases, (5) total parenteral nutrition within past 4 months, (6) hepatotoxic drugs intake, (7) malignancies, (8) DM or (9) pregnancy	No significant difference in alcohol intake among all groups
Meng et al ⁸² 2018 China	Cross-sectional	Total sample = 26,790 Data categorized by soda intake frequency: almost never, <1 cup/week, ≥ 1 cup/week Mean age 41 years 50.5% male	No specific terminology or BMI parameters provided to classify weight. Abdominal adiposity defined as WC ≥ 85 cm (male) or ≥ 80 cm (females)	Abdominal US NAFLD diagnostic criteria: Fatty liver on US in absence of weekly alcohol intake > 140 g (males) and > 70 g (females). Also distinguished between NAFLD with normal ALT or elevated ALT	In fully adjusted logistic regression, soda intake positively associated with NAFLD prevalence (highest vs lowest frequency, NAFLD with normal or elevated ALT) NAFLD + normal ALT OR = 1.26, 95% CI: 1.14-1.40, $P_{trend} < 0.001$

				Participants excluded from study for (1) AFLD, (2) chronic HBV or HCV, (3) autoimmune liver disease, (4) current liver cancer, (5) operation on liver, (6) history of CVD or cancer	NAFLD + elevated ALT OR = 1.32, 95% CI: 1.13-1.53, P _{trend} < 0.0001
Musso et al ⁴⁴ 2007 Italy	Cross-sectional	Total sample = 138 Data categorized into Insulin Sensitive (IS) NAFLD and Insulin Sensitive (IS) control groups Mean age 48-52 73.4% male	Used term non-obese. Defined as BMI < 30 kg/m ² (males) or < 28 kg/m (females). Abdominal obesity defined as WC > 102 cm (males) and > 88 cm (females)	Abdominal US NAFLD diagnostic criteria included (1) elevated ALT and AST ≥ 6 months, (2) US confirmed fatty liver, (3) daily alcohol intake < 20 g (males) and < 10g (females), and (4) no other causes of liver or biliary tract disease (i.e., viral hepatitis, autoimmune disorders, CD, abnormal copper metabolism, α1-antitripsin deficiency, hemochromatosis, abnormal thyroid function, occupational hepatotoxins exposure, use of steatogenic medications or those affecting glucose or lipid metabolism)	No significant difference in alcohol intake between lean IS NAFLD and lean IS control groups
Niemelä et al ³⁵ 2019 Finland	Cross-sectional	Total sample = 22,327 Data categorized by WHO risk drinking levels (grams ethanol/day): Low = 1-40 g/d Medium = 41-60 g/d High = 61-100 g/d Very high > 100 g/day Mean age 45-55 years 48.0% male	No terminology, BMI, or WC parameters specified to classify weight	ALT and GGT Evaluated liver health based on enzymes. Relationship to NAFLD unclear Participants excluded from study for (1) clinical signs of liver disease, (2) ischemic heart or brain disease, or (3) active infection	- Linear increase in abnormal ALT and GGT associated with increasing drinking level risk in all sexes (p < 0.0005) - Low, medium, high, and very high risk drinking levels associated with abnormal GGT compared to abstainers (ORs for low to very high risk, 95% CI) Male OR = 1.61, 3.77, 4.42, 6.73 Female OR = 1.29, 2.45, 3.76 - Medium, high, and very high risk associated with abnormal ALT in males compared to abstainers ORs for medium, high, and very high risk = 2.73, 1.99, 4.29 (95% CI)

					High risk drinking levels associated with risk for abnormal ALT in females OR = 2.52 (95% CI) Note: data for very high risk female group and AST and ALT excluded due to anthropometrics exceeding inclusion criteria
Nishioji et al ²⁰ 2015 Japan	Cross-sectional	Total sample = 3271 Data categorized into non-obese controls, obese controls, Non-obese NAFLD, obese NAFLD groups Mean age 54-63 years 42.2% male	Defined lean BMI < 22 kg/m² and non-obese as BMI < 25 kg/m². No WC parameters provided	Abdominal US No specific NAFLD diagnostic criteria provided Participants excluded from study for (1) presence of HBV and HCV markers (2) alcoholic liver disease (intake ≥20 g/day), (3) autoimmune liver diseases including autoimmune hepatitis, or primary biliary cirrhosis, (4) uncontrolled biliary diseases including bile ductal stone, stenosis, or biliary dilatation	- In adjusted multivariate logistic regression with females, drinking <20 g/d alcohol negatively associated with NAFLD non-obese females, but not in lean or obese females Non-obese females OR = 0.66, 95% CI: 0.44-0.99, p = 0.045 (Data not provided for other groups) - In adjusted multivariate logistic regression with males, alcohol intake < 20 g/d independently and inversely associated with NAFLD in obese males, but not in non-obese or lean males Obese males OR = 0.49, 95% CI: 0.27–0.90, p = 0.022 (data not provided for other groups)
Olubamwo et al ³³ 2019 Finland	Prospective study Mean follow up 18.8 years	Total sample = 1792. Data categorized by FLI (groups were FLI < 30, 30-60, and ≥ 60) Mean age 53 years 100% male	Non-obese used to classify weight but no BMI parameter provided as definition. Abdominal adiposity defined as WC ≥ 120 cm	FLI Evaluated “hepatic steatosis” and “Fatty Liver Disease” (FLD). FLI 30-60 indicated indeterminant fatty liver and FLI ≥ 60 indicated fatty liver. Unclear if considered part of NAFLD diagnosis. Participants excluded for (1) history of physician diagnosed liver or pancreatic disease, (2) history of DM	In Jonckheere trend test, alcohol intake significantly higher in FLI ≥ 60 group compared to FLI < 30 (116 g/week vs 55 g/week, p < 0.0001)

Park and Kang ⁴⁸ 2020 South Korea	Cross-sectional	Total sample = 27,374 Data categorized into groups with or without presence of genetic trait associated with NAFLD risk (minor allele haplotype 22q13 loci) Mean age 54-55 years 35.9% male	Lean defined as BMI < 25 kg/m ² . Abdominal obesity defined as WC > 90 cm (males) and > 85 cm (females)	Abdominal US NAFLD diagnostic criteria: Fatty liver confirmed on US without alcohol intake >40 g/d (males) and >30 g/d (females) Participants excluded from study if "serious disease present"	No significant interaction between those with genetics associated with NAFLD risk and low or high intake of alcohol, coffee, or tea P_{interaction} = 0.448 (alcohol) P_{interaction} = 0.446 (coffee) P_{interaction} = 0.721 (tea)
Sharma et al ⁸⁵ 2020 India	Prospective	Total sample = 100 Data categorized into non-overweight NAFLD and obese NAFLD groups Mean age 38-40 No details provided on sex distribution	Lean, non-overweight, and non-obese used interchangeably. Defined as BMI < 23 kg/m ² . No WC parameters provided.	Abdominal US NAFLD diagnostic criteria: Fatty liver identified in US with absence of the following (1) alcohol intake > 21 drinks/week (males) and >14 drinks/week (females) in past 2 years, (2) use of steatogenic medications, (3) certain hereditary disorders like abetalipoproteinemia, lecithin-cholesterol acyltransferase deficiency, cholesterol ester storage disease and Wolman's disease	Obese NAFLD group had significantly higher intake of aerated soft drinks per month compared to lean NAFLD (Obese vs. lean group for drinks per month) 12±1.7 vs. 17±7.5, p = 0.005
Suomela et al ³⁴ 2015 Finland	Prospective Follow up 3-15 years	Total sample = 1,998 Data categorized into groups: normal weight/normal liver, normal weight/fatty liver, overweight/normal liver, overweight/fatty liver Mean age 42-43 years 45.5% male	Normal weight defined as BMI < 25 kg/m ² . No WC parameters provided.	Abdominal US Evaluated hepatic steatosis. Relationship with NAFLD unclear. No NAFLD diagnostic criteria specified Participants not excluded from study for other secondary causes of fatty liver Defined moderate alcohol intake as < 20 g/day and high intake > 20 g/day	- Lean/fatty liver group had higher percentage of calories from alcohol compared to overweight groups with and without fatty liver (all p = 0.03) - In adjusted multivariate logistic regression, alcohol intake < 20 g/day and > 20 g/day positively associated with fatty liver risk, but higher risk in lean group Alcohol intake < 20 g/day Lean OR = 1.47, 95% CI: 1.21-1.79 Overweight OR = 1.20, 95% CI: 1.08-1.34 Alcohol intake > 20 g/day Lean OR = 3.08, 95% CI: 1.53 - 6.20

					Overweight OR = 1.72, 95% CI: 1.22-2.4 Alcohol intake independently and positively associated with fatty liver with strongest interaction in lean group Lean OR = 1.41, p value = 0.01 Overweight OR = 1.14, p value = 0.1
Takahashi et al ⁵⁷ 2015 Japan	Cross-sectional	Total sample = 8029 Data categorized by drinking status: Non-drinkers (<20 g daily), moderate drinkers (20–50 g daily), and heavy drinkers (>50 g daily) Mean age 47-52 years 71.6% male	Nonobese defined a BMI < 25 kg/m². Visceral adiposity defined as WC > 85 cm (males) and > 90 cm (females)	Abdominal US Evaluated fatty liver. Relationship to NAFLD unclear. No diagnostic criteria specified. Participants excluded from study for (1) HBV or HCV, (2) steatogenic drug use, (3) receiving medical care for metabolic disorders including DM, HTN, and HLD	- Heavy alcohol intake positively associated with fatty liver risk in females but not males (compared to non-drinkers, 95% CI) Female OR = 3.35, p = 0.002 Male OR = 0.953, p = 0.619 In stratified analysis (non-obese vs obese) - Heavy drinking positively associated fatty liver risk in non-obese male and females (compared to non-drinkers, 95% CI) Male OR = 1.286 Female OR = 2.216 - Moderate alcohol intake negatively associated with fatty liver risk in non-obese females, but positively associated in males (compared to non-drinkers, 95% CI) Female OR = 0.393 Data for males not provided - In obese males, moderate and heavy drinking inversely associated with fatty liver risk compared to non-drinkers (compared to non-drinkers, 95% CI) OR = 0.618-0.765 - In obese females, moderate drinking inversely associated with fatty liver risk and heavy drinking positively associated (compared to non-drinkers, 95% CI) Heavy drinking OR = 6.571-8.350 Data for moderate drinking not provided

Tajima et al ⁵⁹ 2017 Japan	Cross-sectional	Total sample = 2444 Data categorized by quartiles of rice, noodle, and bread intake (Q1-Q4) Mean age 52-53 years 40% male	No specific terminology or BMI and WC parameters provided to categorize weight	Abdominal US NAFLD diagnosis based on assumption that fatty liver was related to NAFLD due to participants being excluded from study for (1) alcohol intake ≥ 30 g/d (males) and ≥ 20 g/d (females), (2) self-reported possibility of pregnancy, (3) other self-reported liver diseases, (4) positive or unknown hepatitis B or C serology, (5) history of gastrectomy, (6) use of medication for HLD or DM, (7) use of breast cancer medications, (8) use of hormone replacement therapy, (9) T2DM	No significant linear association between soft drink intake and NAFLD prevalence in all sexes and quartiles of rice, noodle, or bread intake OR = 0.80-1.06, $P_{\text{trend}} = 0.21-0.95$
Tajima et al ⁵⁸ 2020 Japan	Cross-sectional	Total sample = 4579 Data categorized by quartiles of increasing alcohol intake based on percent of kcal (%E) from alcohol (Q1 = 0.5%, Q2 = 3%, Q4 = 7%, Q5 = 15%) Mean age 51-54 years 49.9% male	Non-overweight defined as BMI < 23.0 kg/m ² . No WC parameters provided	Abdominal US Evaluated fatty liver. Relationship to NAFLD unclear. Did not specify NAFLD diagnostic criteria Participants excluded from study for (1) presence of other liver diseases including AFLD, HCV, HBV, liver cirrhosis, and liver cancer, (2) possible pregnancy, (3) history of gastrectomy, (4) currently taking hepatotoxic medications	- Lower fatty liver prevalence associated with low to moderate alcohol intake compared to non-drinkers PR for Q1-Q4 = 0.87, 0.73, 0.72, 0.77 (95% CI, $P_{\text{trend}} = 0.003$) - Lowest fatty liver prevalence associated Q3 (7.2%E from alcohol) - All associations attenuated and not significant after models adjusted for BMI (compared to non-drinkers) PR for Q1-Q4 = 1.04, 0.94, 0.87, 0.92 (95% CI, $P_{\text{trend}} = 0.06$)
Yamada et al ⁶⁸ 2010 Japan	Cross-sectional and retrospective longitudinal (monitored for 5 year period)	Cross-sectional total sample = 63,447 Longitudinal total sample = 10,424 Data categorized by drinking status: (1) non-drinkers, (2) occasional (no definition), (3) daily moderate (23 g/day), (4) daily heavy (46-69 g/day or > 69 g/day)	No specific terminology used to classify weight. Obesity defined as BMI ≥ 25 kg/m ² . No WC parameters provided	Abdominal US Evaluated fatty liver. Relationship with NAFLD unclear. No diagnostic criteria Participants excluded from studies for previous or current history of hepatic disease including autoimmune disorder, HBV or HCV, drug use, or unknown etiology	Cross-sectional study results: - Moderate drinkers had lower fatty liver prevalence than non-drinkers in all sexes ($p < 0.05$). - Occasional, daily moderate, and daily heavy drinking inversely associated with fatty liver in males (compared to non-drinkers, 95% CI) Occasional OR = 0.89 Daily moderate OR = 0.58 Daily heavy drinking OR = 0.57

		Mean age 51-52 years 53.4% male			- Occasional and daily moderate intake inversely associated with fatty liver in females (compared to non-drinkers, 95% CI) Occasional OR = 0.77 Daily moderate OR = 0.53 Heavy drinking inversely associated with fatty liver, but not significant (OR = 0.85, 95% CI: 0.60-1.23) - Longitudinal study results: - Moderate and daily heavy drinkers associated with lower risk for developing new fatty liver (data not provided) - Daily moderate and heavy drinking inversely associated with fatty liver in males (compared to non-drinkers, 95% CI) Daily moderate OR = 0.72 Heavy drinking OR = 0.65 - No significant association between occasional, daily moderate, or daily heavy drinking and fatty liver risk in females
Yamamoto et al ⁶⁵ 2023 Japan	Cross-sectional	Total sample = 464 Categorized into groups non-NAFLD and NAFLD group. Further categorized into groups with APOC3 T-455C genotypes (TT, TC, and CC) Mean age 62 years 37.1% male	Nonobese defined as BMI < 25 kg/m ² . No WC parameters provided	Abdominal US No NAFLD diagnostic criteria specified besides US confirmed fatty liver. Participants excluded from study for (1) history or treatment of hepatitis, (2) daily alcohol intake >30 g (males) or >20 g (females)	- No significant interaction between NAFLD and alcohol intake in those with APOC3 genotypes - Alcohol intake was not associated with NAFLD risk in any of the genotypes

Yu et al ⁸¹ 2014 China	Prospective study Follow up every 2-3 years	Total sample = 56,195 Data categorized by sex and quintiles of increasing choline intake (Q1-Q5) Mean age 50-54 years 33.4% male	Normal weight defined as BMI < 25 kg/m ² . No WC parameters provided.	Participant self-report of diagnosis via abdominal US NAFLD diagnostic criteria: Proof of fatty liver diagnosis by physician and alcohol intake ≤ 28 g/d (males) or ≤ 14 g/d (females) at baseline Participants excluded from study if reported hepatitis, CVD, or cancer at baseline	• No association between alcohol intake and NAFLD risk (data not provided) • Alcohol intake had no effect modification on inverse association between choline and NAFLD risk
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3.7 Physical Activity and Lean NAFLD

A total of 18 studies examined physical activity and how it relates to NAFLD or fatty liver risk. Nine studies observed an inverse association between physical activity and NAFLD or fatty liver risk and ten studies, while ten studies reported no association. Detailed data are shown in Table 3.4.

Nine studies observed an inverse relationship between physical activity and NAFLD or fatty live risk^{10,45,49,53,61,69,77,81,83}. Four studies specifically analyzed the association between physical activity measured in MET minutes per week^{49,53,77,81}. This included one study that reported approximately 1500-1700 MET min of total physical activity or 1400–1500 MET minutes of leisure physical activity were inversely associated with NAFLD risk compared to lower MET minute ranges (HR = 0.57–0.66)⁴⁹. Another study reported similar results with at least 1400 MET minutes of physical activity/week, but this was among participants with high intake of vegetables (HR = 0.79)⁷⁷. A third study reported an inverse relationship between both minimal physical activity (defined as at least 600 MET minutes/week) and Health Enhancing Physical Activity (at least 1500 MET minutes/week) and fatty liver prevalence (PR = 0.80–0.94). This association remained even in subgroup analysis comparing participants with BMI < 25 kg/m² (PR = 0.74–0.92) and BMI < 23 kg/m² (PR = 0.72–0.90)⁵³. One study reported lower physical activity (90–155 MET minutes/week) were inversely associated with NAFLD risk, though this was only observed in female participants and not males (OR = 0.87–0.88)⁸¹.

Three studies categorized physical activity as moderate or vigorous intensity and also observed an inverse association between physical activity and NAFLD risk^{45,61,69}. Two studies reported an inverse association between at least 90–150 minutes of moderate intensity or vigorous intensity physical activity and NAFLD risk (OR = 0.62–0.81)^{45,69}. One of these studies

also assessed the association between physical activity and NAFLD risk based on frequency (3–4 days/week vs ≥ 5 days/week), duration of usual exercise habits (< 1 year or ≥ 1 year), and intensity (moderate and vigorous intensity). General trends suggested that both lower and higher levels of frequency, duration, and intensity categories were inversely associated with NAFLD risk compared to not exercising except in individuals with BMI < 19.6 and BMI = 20.7–21.6 (ORs for all levels of frequency = 0.49–0.72, duration = 0.37–0.80, and intensity = 0.42–0.72)⁴⁵. The remaining study reported on the effect of physical activity in mediating the potential association between alcohol intake and fatty liver risk. Researchers reported that low or moderate intensity physical activity at least three times per week was associated with significantly reducing fatty liver risk in participants categorized as never to moderate drinkers (HR = 0.82 for low intensity and 0.56 for moderate intensity). Completing vigorous intensity physical activity two and three times weekly was associated with reducing fatty liver risk by almost half in never to moderate drinkers (HR = 0.55–0.57). However, there was no significant association between any frequency or intensity of physical activity and fatty liver risk in heavy drinkers⁶¹.

Results from four other studies suggested beneficial effects of physical activity for reducing NAFLD risk by identifying negative outcomes associated with sedentary behaviors^{10,49,53,83}. This included two studies reported sitting time ≥ 7 –10 hours/day was positively associated with NAFLD prevalence independent of physical activity (PR = 1.09)^{53,83}. Additionally, a cross-sectional study that observed physical activity that was less than moderate intensity and 2 hours per week was an independent predictor of NAFLD in lean participants (OR = 0.063)¹⁰. A longitudinal study identified that among participants with a significant reduction in physical activity at follow up compared to baseline data had a higher risk of developing NAFLD (HR = 1.59)⁴⁹.

In contrast, ten studies reported no association between physical activity and NAFLD or fatty liver risk^{9,10,20,29,31,33,34,48,55,85}. This included four studies using study group comparisons that observed no significant difference in physical activity levels when comparing lean participants with NAFLD, NASH, or fatty liver to lean participants without these conditions^{9,31,33,85}. One of these studies reported lean individuals with or without NASH had higher amounts of physical activity compared to obese participants with or without NASH, but data was not provided for comparison and this trend is more suggestive of the protective effects of physical activity against obesity³¹. Six other studies reported no association between physical activity and NAFLD or fatty liver risk using logistic regressions^{10,20,29,34,48,55}. The amount and/or type of physical activity assessed in these studies varied significantly depending on study design and methods. Two studies only evaluated walking as physical activity and reported no association with NAFLD risk in lean participants regardless of walking speed, frequency, and/or duration^{10,20}. Another study reported no significant interaction between high or low physical activity (defined as less than or greater than 90 minutes of activity daily) and genetic factors associated with increased NAFLD risk⁴⁸. Interestingly, one cross-sectional study reported regular physical activity (defined as at least one 30 minute session weekly) was not associated with elevated ALT and GGT, but was positively associated with elevated AST (OR = 1.482)⁵⁵. Finally, a pre and post intervention study reported no effect of endurance training (up to 180 minutes/week of moderate intensity exercise in the final weeks of intervention) on ALT and overall liver fat content in lean females and males. However, the endurance training intervention had a reducing effect on GGT in lean males (p = 0.01 for change in GGT after intervention), but not lean females²⁹.

Table 3.4. Physical activity risk and protective factors in lean NAFLD or fatty liver

Author	Study Design	Study characteristics	Anthropometric measures	NAFLD Diagnostic Criteria	Physical Activity Definitions	Main Findings
Bae et al ⁴⁵ 2012 South Korea	Cross-sectional	Total sample = 72,359 Data categorized into non-exercise and exercise group. Exercise group further categorized into BMI deciles Mean age 42 years 53.8% male	Normal weight defined as BMI < 23 kg/m ² . No WC parameters provided	Abdominal US NAFLD diagnostic criteria not specified beyond imaging details. Participants excluded from study for (1) daily alcohol intake > 30 g (all sexes), (2) DM, (3) HBV or HCV, (4) US findings indicating cirrhosis, hepatocellular carcinoma, or hepatic mass, (5) history of malignancy or hypo- or hyperthyroidism	Exercise group defined as completing moderate intensity PA at least 3 days/week, at least 30 minutes in duration, and at least the past 3 months	- In fully adjusted models where BMI stratified into deciles, exercise negatively associated with NAFLD risk in all BMI deciles BMI < 19.6 and 20.7-21.6 (compared to no exercise, 95% CI) OR (BMI < 19.6) = 1.31 OR (BMI 20.7-21.6) = 0.91 ORs (other BMI deciles) = 0.62-0.78 - Exercise group had lower risk for elevated liver enzymes compared to non-exercise group (fully adjusted model, 95% CI) AST OR = 0.85 ALT OR = 0.74 - Prevalence of NAFLD differed among BMI deciles depending on frequency, duration, and intensity with no specific trends identified
Deng et al ⁶⁹ 2021 China	Cross-sectional	Total sample = 2981 Data categorized by HLS range of 0-6. Mediterranean diet part of HLS. Mean age 61 years 32% male	Normal weight defined as BMI 18.5-23.9 kg/m ² . Abdominal adiposity defined as WC ≥ 85 cm (males) or ≥ 80 cm (females)	Abdominal US NAFLD diagnostic criteria not specified Participants excluded from study for (1) history of malignancy, hyperthyroidism or viral hepatitis, (2) alcohol intake ≥ 30 g/d (males) or ≥ 20 g/d (females)	Physically active defined as moderate or vigorous PA ≥ 150 minutes per week. Evaluated as part of Healthy Living Score (HLS)	Physically active status associated with lower NAFLD risk in both sexes (compared to not being physically active) OR = 0.81, 95% CI 0.69-0.94, p-value = 0.006

Devries et al ²⁹ 2008 Canada	Uncontrolled pre-post intervention study 12 weeks duration	Total sample = 41. Data categorized into lean and obese groups. All completed 12-week endurance training intervention Mean age 38-41 years 43.9% male	Lean used to identify normal weight individuals. No BMI or WC parameters provided as definition	CT scan Evaluated hepatic fat content. Relationship to NAFLD unclear. No diagnostic criteria specified. Participants excluded from study for (1) T2DM, (2) HTN requiring more than one medication for management, (3) smoking (4) daily alcohol intake > 25 g (all sexes)	12-week moderate intensity endurance training intervention. Progressed from 15-30 minutes cycling twice weekly to 60 minutes cycling three times per week	- Endurance training intervention had no significant effect on hepatic fat content in both lean and obese groups. - Endurance training significantly lowered GGT in lean males (p = 0.01), but not in lean females - No effect on ALT in lean males and females
Duarte et al ³¹ 2018 Brazil	Cross-sectional	Total sample = 23 Data categorized into groups (1) lean NASH, (2) overweight NASH, (3), obese NASH, (4) lean controls, (5) obese controls Median age 30-53 years 52% male	Lean defined as BMI < 25 kg/m ² . No WC parameters provided.	Liver biopsy NASH diagnostic criteria: Liver histology and absence of (1) daily alcohol daily intake >30 g (males) and >20 g (females) (2) drug addiction (3) HBV or HCV, (4) schistosomiasis, (5) detectable serum autoantibodies associated with liver disease, (6) altered serum ceruloplasmin levels, and (7) hemochromatosis	No details provided	Lean control and lean NASH groups had higher exercise than obese controls, overweight NASH, and obese NASH participants (no data or statistical analysis provided, reported all participants exercised < 90 minutes/day)
Iwata et al ⁵⁵ 2013 Japan	Cross-sectional	Total sample = 1809 Mean age 35 years 100% male	No specific weight terminology used. No BMI or WC parameters provided to categorize weights	Liver enzymes (AST, ALT, GGT) Evaluated "hepatocellular injury". No NAFLD diagnosis specified Participants excluded from study for history of	Regular exercise defined as at least one 30-minute session at least once weekly	- Regular exercise positively associated with elevated AST (compared to no regular exercise) OR = 1.482, 95% CI: 1.052-2.088 - No association between regular exercise and elevated ALT and GGT

				(1) stroke, (2) ischemic heart disease, (3) chronic renal failure, (4) alcohol dependency diagnosed by psychiatrist (5) liver cirrhosis or cancer (6) HBV or HCV		
Kwak et al ⁴⁹ 2017 South Korea	Longitudinal cohort study Followed from 2007-2008 to 2011-2013, median follow up duration 4.42 years	Total sample = 1373 Data categorized into quartiles of increasing total physical activity (MET-min/week) Mean age 51 years 51.6% male	No specific terminology, BMI, or WC parameters provided to classify weight	Abdominal US NAFLD diagnostic criteria: Fatty liver confirmed by US and the absence of (1) daily alcohol intake > 30 g (males) and > 20 g (females), (2) positive tests for HBV or HCV, (3) other known causes of chronic liver disease, (4) steatogenic medication use	Total PA included both leisure, domestic, work-related, and transport-related PA Exercise quartiles reported in MET-min/week. Q1 = 0-248 (female) or 0-414 (male) Q4 ≥ 1533 (female) or 1741 (male) MET-min/week	In fully adjusted cox-regression model: - Baseline total PA inversely associated with NAFLD incidence (Q4 vs Q1) HR = 0.66, 95% CI: 0.46-0.94, P_{trend} = 0.022 - Baseline leisure PA inversely associated with NAFLD incidence (Q4 vs Q1) HR = 0.57, 95% CI: 0.37-0.87, P_{trend} = 0.010 In fully adjusted model with follow up data: - Not sustaining PA levels from baseline associated with NAFLD risk (comparing highest to lowest change in PA from baseline) HR = 1.59, 95% CI: 1.11-1.27, P_{trend} = 0.011
Kwak et al ¹⁰ 2018 South Korea	Cross-sectional	Total sample = 209 Data categorized into groups (1) non-obese NAFLD, (2) non-obese controls, (3) obese NAFLD, (4) obese controls Age 39-41 years	Non-obese and normal weight used interchangeably. Defined as BMI < 25 kg/m ² . No WC parameters provided	Abdominal CT scan NAFLD diagnostic criteria: fatty liver in absence of daily alcohol intake > 30 g (males) or > 20 g (females) in past two years Participants excluded from study for (1)	Vigorous PA = running, climbing, bike, fast swimming, football, basketball, jump rope, squash, singles tennis Moderate PA = slow swimming, doubles tennis, volleyball,	In fully adjusted logistic regression, physical activity less than moderate intensity and 2 hours/week independent predictor of NAFLD in lean NAFLD participants OR for exercise 2 hours/week = 0.063, 95% CI: 0.007-0.534, p = 0.011

		No data on sex distribution provided		steatogenic medications use in past month (including herbal and prescription medicines), and/or (2) HBV, HCV, or autoimmune hepatitis	badminton, table tennis	Lean controls and NAFLD group did not differ in frequency (days/week) and amount of walking (min/week)
Nishioji et al ²⁰ 2015 Japan	Cross-sectional	Total sample = 3271 Data categorized into non-obese controls, obese controls, Non-obese NAFLD, obese NAFLD groups Mean age 54-63 years 42.2% male	Defined lean BMI < 22 kg/m² and non-obese as BMI < 25 kg/m². No WC parameters provided	Abdominal US No specific NAFLD diagnostic criteria provided Participants excluded from study for (1) presence of HBV and HCV markers (2) alcoholic liver disease (intake ≥20 g/day), (3) autoimmune liver diseases including autoimmune hepatitis, or primary biliary cirrhosis, (4) uncontrolled biliary diseases including bile ductal stone, stenosis, or biliary dilatation	PA measured in terms of walking speed, frequency, and duration	In adjusted logistic regression: - No association between walking speed and NAFLD risk in lean females and males - Walking speed negatively associated with NAFLD in obese females OR = 0.54, 95% CI: 0.31–0.93, p = 0.029
Olubamwo et al ³³ 2019 Finland	Prospective study Mean follow up 18.8 years	Total sample = 1792 Data categorized by FLI (groups were FLI < 30, 30-60, and ≥ 60) Mean age 53 years 100% male	Non-obese used to classify weight but no BMI parameter provided as definition. Abdominal adiposity defined as WC ≥ 120 cm	FLI Evaluated “hepatic steatosis” and “Fatty Liver Disease” (FLD). FLI 30-60 indicated indeterminant fatty liver and FLI ≥ 60 indicated fatty liver. Unclear if considered part of NAFLD diagnosis Participants excluded for (1) history of physician diagnosed liver or pancreatic disease, (2) history of DM	No details provided on data collected for PA, but reported as calories expended per day	In Jonckheere trend test, no significant difference in physical activity between FLI ≥ 60 and FLI < 30 groups 136 vs 129 kcal expended/day

Park and Kang ⁴⁸ 2020 South Korea	Cross-sectional	Total sample = 27,374 Data categorized into groups with or without presence of genetic trait associated with NAFLD risk (minor allele haplotype 22q13 loci) Mean age 54-55 years 35.9% male	Lean defined as BMI < 25 kg/m². Abdominal obesity defined as WC > 90 cm (males) and > 85 cm (females)	Abdominal US NAFLD diagnostic criteria: Fatty liver confirmed on US in absence of alcohol intake >40 g/d (males) and >30 g/d (females) Participants excluded from study if “serious disease present”	Low physical activity defined as 90 min/day	No significant interaction between low or high physical activity and NAFLD risk in those with genetic trait associated with NAFLD
Ryu et al 2015 South Korea	Cross-sectional	Total sample = 139,056 Data categorized by (1) Sitting time: < 5, 5-9, or ≥ 10 hours/day (2) Physical activity status: inactive, minimally active, Healthy Enhancing Physical Activity (HEPA) Mean age 40 years 52.4% male	Defined “non-obese” as BMI < 25 kg/m². No parameters provided for WC	Abdominal US NAFLD diagnostic criteria not specified beyond imaging details Participants excluded from study for (1) daily alcohol intake ≥ 30 g (male) or ≥ 20 g (female), (2) positive HCV or HBV test, (3) steatogenic medication use in past year, (4) known liver disease, (5) history of malignancy	PA measure in METs-min/week Minimally active: (1) ≥ 20 minutes vigorous PA for at least 3 days, (2) ≥ 30 minutes of moderate intensity PA or walking at least 5 days/week, or (3) ≥ 5 days of any combination of walking and moderate or vigorous intensity activities that achieves ≥ 600 METs-min/week HEPA definition: (1) vigorous intensity activity ≥ 3 days/week that achieves ≥ 1500 MET-min/week, or (2) any combination of walking, moderate, or	In fully adjusted Poisson regression: - Sitting time positively associated with NAFLD prevalence independent of physical activity compared to < 5 h/day sitting time (95% CI, $P_{trend} < 0.001$) PRs (5-9 h/d) 1.04 PR (≥ 10 h/d) = 1.09 - Higher PA levels inversely associated with NAFLD prevalence compared to inactive group (95% CI, $P_{trend} < 0.001$) Minimally active PR = 0.94 HEPA PR = 0.80 - Sitting time positively associated with NAFLD prevalence in subgroup analysis of BMI categories (95% CI, $P_{trend} < 0.001$) BMI < 23 Minimally active PR = 0.90 HEPA PR = 0.72

					vigorous intensity activity that achieves ≥ 3000 MET-min/week	BMI < 25 Minimally active PR = 0.92 HEPA PR = 0.74 HEPA associated with higher NAFLD prevalence if paired with ≥ 10 h/d sitting time (no data provided)
Sharma et al ⁸⁵ 2020 India	Prospective	Total sample = 100 Data categorized into non-overweight NAFLD and obese NAFLD groups Mean age 38-40 years No details provided on sex distribution	Lean, non-overweight, and non-obese used interchangeably. Defined as BMI < 23 kg/m ² . No WC parameters provided.	Abdominal US NAFLD diagnostic criteria: Fatty liver identified in US with absence of the following (1) alcohol intake > 21 drinks/week (males) and >14 drinks/week (females) in past 2 years, (2) use of steatogenic medications, (3) certain hereditary disorders like abetalipoproteinemia, lecithin-cholesterol acyltransferase deficiency, cholesterol ester storage disease and Wolman's disease	PA assessed based on aerobic exercise and average min/week of walking, cycling, or treadmill	No significant difference in aerobic exercise between obese NAFLD and lean NAFLD groups (data not provided stating no uniform PA pattern in participants)
Suomela et al ³⁴ 2015 Finland	Prospective Follow up 3-15 years	Total sample = 1,998 Data categorized by weight (normal or overweight) and liver status (normal liver or fatty liver) Mean age 42-43 years 45.5% male	Normal weight defined as BMI < 25 kg/m ² . No WC parameters provided.	Abdominal US Evaluated hepatic steatosis. Unclear if part of NAFLD diagnosis. No NAFLD diagnostic criteria specified Participants not excluded from study for other secondary causes of liver disease	Reported as Physical Activity Index (considers PA duration, intensity, and frequency)	PA independently and inversely associated with fatty liver in overweight group, but not in normal weight group Overweight OR = 0.76, 95% CI:0.63-0.90 Note: OR for normal weight group not provided

Tsunoda et al 2014 Japan	Prospective cohort study Mean follow up at 4.4 years	Total sample = 10,146 Data categorized by drinking frequency (never-moderate or heavy drinkers) and PA frequency (< 1x, 1x, 2x, or ≥ 3x/week) Mean age 48 years 48.7% male	No specific terminology, BMI, or WC parameters to classify weight	Abdominal US Evaluated fatty liver. Relationship to NAFLD unclear. No diagnostic criteria specified. Participants excluded from study for (1) history of liver disease including HBV, HCV, cirrhosis, or hepatic haemangioma (2) use of steatogenic medications	Measured using questionnaire evaluating frequency and intensity. Low intensity exercise = 3-5 METs, moderate intensity = 5-7 METs, vigorous intensity ≥ 7 METs. Minimum 10 minutes exercise duration	• Never-moderate drinkers paired with ≥3x/week low-intensity or moderate intensity PA associated with reduced NAFLD risk (compared to exercising < 1x/week, 95% CI) Low intensity HR = 0.82 Moderate Intensity HR = 0.56 • Never-moderate drinkers paired with vigorous intensity PA for 2x or 3x/week associated with reduced NAFLD risk (compared to exercise < 1x/week, 95% CI) HR (2x/week) = 0.57 HR (3x/week) = 0.55 • No significant associations between PA frequency and intensity and NAFLD risk in heavy drinkers
Yabe et al ⁹ 2023 Japan	Cross-sectional	Total sample = 169 Data categorized into non-obese NAFLD and non-NAFLD groups Mean age 59-62 years 36.7% male	Lean and non-obese used interchangeably. Defined as BMI < 25 kg/m ² . No WC parameters provided.	Abdominal US, US elastography, and/or self-report No NAFLD diagnostic criteria specified. Participants excluded from study for (1) daily alcohol intake >30 g (males) or 20 g (females), (2) liver diseases including HCC, HBV, HCV, liver cirrhosis, PBC, primary sclerosing cholangitis, autoimmune hepatitis	Physical Activity Level (PAL) measured intensity of daily activities based on calorie expenditure. Low = 1.5, normal = 1.75, or high = 2.0 Exercise (Ex) measured amount of exercise based on METs-hours/week	• No significant difference in PAL and Ex between lean NAFLD and lean control group Lean NAFLD vs lean controls PAL: 1.6 ± 0.3 vs. 1.7 ± 0.5, p = 0.054 • Ex: 8.0 ± 14.1 vs. 11.5 ± 21.7, p = 0.485
Wei et al ⁸³ 2016 China	Cross-sectional	Total sample = 2054 Data categorized by tertile of sitting	No specific terminology, BMI, or WC parameters provided to	FLI NAFLD diagnostic criteria: FLI > 60 and absence of the following	PA measured with MET-h/week Tertiles of sitting time: T1 = 2.2-5.0	• In adjusted multivariate logistic regression, longer sitting time (> 7.1 h/day) associated with NAFLD prevalence independent of

		time in hours/day (T1-T3) Mean age 57-58 years 100% male	classify weight. Defined obese as BMI ≥ 25 kg/m ²	(1) previous or current alcohol intake > 20 g/d or 140 g/week, (2) previous or current HBV or HCV infection, biliary diseases, autoimmune, CD and/or other chronic liver diseases	h/d, T2 = 5.0-6.9 h/d, T3 > 7.1 h/d	physical activity (T3 vs. T1) OR 1.09; 95% CI: 1.04 to 1.67 • Association no longer significant in final model adjusted for inflammation (T3 vs T1) OR = 1.03, 95% CI: 0.92 to 1.84
Yu et al ⁸¹ 2014 China	Prospective study Follow up every 2-3 years	Total sample = 56,195 Data categorized by sex and quartiles of increasing PA (Q1-Q4) Mean age 50-54 years 33.4% male	Normal weight defined as BMI < 25 kg/m ² . No WC parameters provided	Self-reported by participants by providing proof of NAFLD diagnosed by physician using abdominal US NAFLD diagnostic criteria: US confirmed fatty liver and alcohol intake ≤ 28 g/d (males) or ≤ 14 g/d (females) at baseline Participants excluded from study if reported hepatitis, CVD, or cancer at baseline	PA categorized into quartiles of increasing median MET-h/week Q1 = 58.8 Q2 = 86.4 Q3 = 112.3 Q4 = 155.8	• All levels of physical activity inversely associated with NAFLD risk in females but not in males (compared to Q1, 95% CI, p < 0.001) Female ORs (Q2-Q4) = 0.87, 0.88 0.88
Zhang et al ⁷⁷ 2021 China	Prospective cohort study Median follow up 4.2 years	Total sample = 17,360 Median age 37 years 43% male	No BMI or WC parameters provided to define lean	Abdominal US NAFLD diagnostic criteria: Fatty liver confirmed by US and absence of following (1) weekly alcohol intake > 210 g (males) and > 140 g (females), (2) other liver diseases including HBV, HCV, HCC, autoimmune liver disease, liver cirrhosis	PA defined as MET hour/week. Higher PA defined as ≥ 23 MET hour/week and lower PA defined as < 23 MET hour/week	• PA levels ≥ 23 MET hours/week combined with highest quartile of vegetable rich dietary pattern associated with decreased NAFLD risk NAFLD (compared to lowest quartile of vegetable intake) HR = 0.79, 95% CI: 0.65, 0.96, P _{trend} = 0.03

Chapter 4 - Discussion

To our knowledge, this is the first scoping review reporting on dietary and physical activity risk and protective factors in lean individuals with NAFLD. The aim of the review was to describe and collate research on this topic, define key terms and definitions, and identify future research opportunities. Overall, the current body evidence provides data on a broad range of topics including associations between specific diets, macronutrients, micronutrients, beverages, and physical activity and lean NAFLD risk. However, very few definitive conclusions can be made about potential dietary or physical activity risk and protective factors for lean NAFLD due to the lack of consensus in the research and limited randomized controlled trials and/or prospective studies in the body of evidence. The published research was also hindered by lack of racial diversity of studied populations, heterogeneity in key terms and definitions, and high risk of bias. Nonetheless, this scoping review was able to identify some key findings about dietary and physical activity risk and protective factors associated with lean NAFLD. Reviewing these key findings and the research limitations can be used to identify many opportunities for future research.

4.1 Key findings: Dietary and Physical Activity Risk and Protective Factors

As one key finding in the research examining the influence of specific diets and food groups, it can be hypothesized that diets higher in vegetables (especially leafy green vegetables) intake, and lower animal-based proteins (especially red meat and organ meats), sodium, and processed foods may be beneficial for reducing NAFLD risk in lean populations. This hypothesis is based on several higher quality and/or larger-scale studies that showed positive associations between diets high in instant noodles, sodium, red meat, poultry, organ meats, and other processed products and NAFLD prevalence or risk^{9,27,46,48,55,55,73,77–80}. Additionally, several

studies observed inverse relationship between NAFLD risk in lean participants and higher intake of vegetables, whole grains, and diets encouraging higher vegetable intakes like DASH diet or those with lower inflammatory diet scores^{18,38,71,72,74–76}. However, it is important to note that several studies provided results that contradict these findings^{27,33,47,60,69,70,75,84,86}. Interestingly, some studies observed that vegetarian or Mediterranean diets, which promote higher intake of vegetables, whole grains, and reduced intake of red meat and/or other animal-based proteins, indicated there was no association between these diets and NAFLD risk^{47,69,75,86}. These inconsistent results could be due to differences in sample sizes, population characteristics, and/or overall study quality. In particular, the contradicting results involving the Mediterranean diet (either having no association or an inverse association) may be a result of differences in ethnicity of the study population and/or how fatty liver was identified. All the studies that found no significant association between Mediterranean diet and NAFLD risk were based in Asia and used abdominal ultrasound to identify NAFLD, while the one study that observed an inverse association was based in Switzerland and used FLI^{38,69,75}.

A key finding related to research on specific nutrient intake was that the influence of macronutrient, micronutrient, other nutritional compounds (i.e., cholesterol, dietary fiber) intake on lean NAFLD risk cannot be determined based on current evidence. This finding was based on the inconsistencies observed in the literature regarding the association between each macronutrient (and their subtypes) and NAFLD or fatty liver risk in lean individuals. Additionally, many of the studies involved small sample sizes and/or lacked quality due design and methods that contributed to high risk of bias. For example, while six studies observed a positive association between carbohydrate intake and lean NAFLD risk, three of the studies had small sample sizes and/or were poor quality^{10,48,50,59,64,84}. A comparison of carbohydrate intake

among study groups also showed inconsistent results where carbohydrate intake was either lower, higher, or no different than lean controls and/or obese NAFLD participants^{30,31,44,50,63,65,66,70,84}. Results on protein intake were more consistent in indicating no association between protein intake and lean NAFLD risk. However, it is challenging to have confidence in the results because among the ten studies showing this association, only four were of higher quality with larger sample sizes^{44,48,70,81}. The remaining studies had small sample sizes and/or were poor quality due to design and methods that increased risk for bias^{10,31,34,63,65,66,84}. Similarly, research on the influence of fat and fat subtypes on NAFLD risk lacked consensus and were hindered by small sample sizes and/or poorer quality designs^{10,31,63,64,66,84}. Even among the higher quality studies, the association between total fat intake and some fat subtypes (i.e., MUFA, SFA, and PUFA's) and NAFLD risk was unclear due to inconsistent results^{44,48,50,62,70,81}. When considering other topics related to specific nutrient intakes including vitamins, minerals, cholesterol, and dietary fiber, no definitive conclusions could be made due to inconsistent results, and the overall low quantity and quality of the research. The research on cholesterol and individual vitamins or minerals either was limited in quantity (only one to two studies reported on the nutrient) or if multiple studies were involved, they were usually studies that drew conclusions based on a comparison of intake among study groups and often providing contradicting results^{10,18,44,63-66,70,81}. The exceptions were vitamin C, vitamin E, and dietary fiber where there were multiple studies that reported on these nutrients and all found no differences in intake among all study groups^{10,31,44,48,64,66,70}.

The research on alcohol intake and NAFLD risk lacked consensus and highlights the complexity of the association between this dietary habit and lean NAFLD. There was almost an equal number of studies that indicated alcohol intake had either no association, a positive, or

negative association with NAFLD or fatty liver risk. Even when comparing different levels of alcohol intake, the associations with NAFLD or fatty liver risk were inconsistent. For example, lower amounts of alcohol intake (defined as daily intake 1–40 g, < 20 g, or < 20–30 g for females and < 30–40 g for males depending on the study) were noted to either have a positive, negative, or no association with NAFLD or fatty liver risk^{34,35,48,52,58,65,67}. The same pattern was observed when considering moderate to high alcohol intake, which was defined as daily intake > 20 g/day, 20–50 g, 30–60, or ≥ 60 g depending on the study^{20,35,55–58,67,68}. Some differences in results can be attributed to smaller sample sizes or lower quality designs^{20,34,44,55,56,65,68}, but there was disagreement even among the higher quality studies with large sample sizes^{48,52,58,70,81}. Differences in results could also be related to how some studies did not examine higher levels of alcohol intake or used broader definitions of “high” alcohol intake such any intake greater than 20 grams/day. For example, one study found no association between moderate alcohol intake (10–40 g in males and 10–30 grams females), but did not evaluate any amount of alcohol intake greater than 40 g/day (males) or 30 g/day (females)⁴⁸. This makes it unclear if alcohol intake was not associated with NAFLD risk because the amount evaluated was not excessive, or if there were other reasons contributing to this result.

Despite the lack of consensus on the overall association between alcohol and NAFLD risk in lean individuals, the other key finding from the review of evidence was how the relationship can be potentially influenced by race, biological sex, and/or level of leanness in participants. Interestingly, the majority of the research on this topic was conducted in Asia populations and provided inconsistent results. However, when considering the small number of studies not conducted in Asia, the results were slightly more consistent. This was apparent in the three studies conducted in Finland that observed a positive association between alcohol intake

and fatty liver risk regardless of the amount of alcohol examined and methods used to evaluate fatty liver (abdominal ultrasound, FLI, and liver enzymes)^{33–35}. Although the total number of studies was small, it suggests that the association between alcohol intake and NAFLD or fatty liver can be clearer in some races than others. As noted in the results section, some studies reported differences in outcomes based on sex and/or body weight status. Two studies reported moderate alcohol intake to be inversely associated with NAFLD risk in females, but was either positively associated or had no association with NAFLD in males^{20,57}. Another study reported heavy drinking was positively associated with NAFLD in males and females, but the association was not significant in females⁶⁸. These variances suggest that potentially females and males respond differently to alcohol and the necessity of tailoring alcohol intake guidelines to biological sexes. Additionally, four other studies reported that when results were stratified into more specific BMI groups, there was a higher NAFLD risk or prevalence of fatty liver with moderate to alcohol consumption (defined as > 20 g/day or 10 to < 20 g/day) in lean participants compared to overweight or obese participants^{20,34,52,57}. One study further noted that an inverse association between alcohol intake and NAFLD risk was observed in female participants with a BMI < 25 kg/m², but not in females with BMI < 22 kg/m² or males in either BMI category²⁰. This might suggest that there can be variation in alcohol effects even among lean individuals as well as when compared to overweight and/or obese individuals. These factors may need to be considered when establishing appropriate alcohol intake limits for NAFLD diagnostic criteria^{20,34,52,57}.

Key findings associated with physical activity and NAFLD or fatty liver risk in lean populations were surprisingly inconsistent. Despite a general consensus about the beneficial effects of physical activity for chronic disease prevention^{88,89}, this scoping review identified

almost an equal number of studies that reported physical activity was either inversely associated^{10,45,49,53,61,69,77,81,83} or had no association^{9,20,29,31,33,34,48,55,85} with NAFLD or fatty liver risk in lean populations. The inconsistent results can likely be attributed to differences in study characteristics and methodology. The studies that reported no association between physical activity and NAFLD or fatty liver risk were more likely to be poorer quality, involved smaller sample sizes, and/or evaluated physical activity that was below the intensity, duration, and frequency examined in the studies that showed protective effects of physical activity for NAFLD^{9,20,29,31,33,34,55}. Additionally, four studies identified no association between physical activity and NAFLD or fatty liver risk based on study group comparisons where there was no significant difference in physical activity between lean participants with or without NAFLD or fatty liver. However, the physical activity data for both of these groups indicated that participants had lower physical activity levels compared to the participants in the studies that identified an inverse association between physical activity and NAFLD risk^{9,31,33,49,53,69,77,85}. In contrast, the nine studies that observed an inverse relationship between physical activity and NAFLD risk involved higher quality studies and larger sample sizes (five studies had sample sizes ranging from 10,176 to 139,056 participants)^{45,53,61,80}. These studies also mostly examined physical activity that was moderate intensity, at least three days a week, and/or met the minimum MET minutes/week recommended by the CDC (at least 500–1000 MET min/week or approximately $\geq$ 150 minutes/week of moderate intensity exercise)^{10,45,49,53,61,69,77,90}. Some studies observed additional risk reduction benefits as intensity, duration, and frequency increased beyond these parameters^{45,61}. These results were also reinforced by studies that indicated a the lack of physical activity was associated with increased NAFLD prevalence^{53,83}. Based on the results from the higher quality studies with larger sample sizes, it can be hypothesized that regular moderate

intensity physical activity is likely protective against lean NAFLD. Nonetheless, more research is needed due to the lack of consensus in the total research and some studies that reported inverse associations between NAFLD risk had limitations including having a smaller sample size and/or not accounting for dietary intake^{10,45,49,53,69}.

4.2 Key findings: Study Quality and Risk of Bias

A common theme identified in the current body of evidence was the overall lack of high-quality studies, and high risk of bias due to methodology and failure to account for all confounding variables. This scoping review revealed that there are no randomized controlled trials on this topic, which is a study design that is considered to have the least amount of bias and can be used to infer causality. The studies were predominantly observational in nature and mostly cross-sectional or prospective studies, which cannot determine causality, and have higher risk for bias. As previously noted in the study characteristics section of Chapter 3, many of the studies lacked details on data collection methods and/or failed to account for multiple confounding factors^{9,18,20,31,33–35,39–41,47,48,50,53–56,58,61–63,65,67–69,71,72,74,75,80,81,83–86}. Some studies also did not provide data for certain reported results, presented results that were not well supported statistically, and/or only discussed results from partially adjusted statistical models rather than the fully adjusted models that accounted for confounders including BMI^{20,45,57,64,81,84–86}. The lack of transparency on any of these details can contribute to high risk of bias and lead to results with questionable validity. Additionally, the methodology in the studies also lacked clarity due to heterogeneity in key terms and definitions related to body weight categorization, NAFLD diagnosis, and excessive alcohol intake. Without clear and consistent definitions of any of these terms, it can be challenging to determine if the population being studied is representative of lean individuals with NAFLD. For example, confusion can arise when researchers utilize terms such

as “fatty liver” or “hepatic steatosis” without specifying whether these terms were considered as part of a NAFLD diagnosis. Because NAFLD refers to a spectrum of conditions ranging from simple steatohepatitis to liver cirrhosis, researchers needed to be clear when using the term fatty liver to clarify whether participants fell within this spectrum and were representative of the population of interest^{2,4,5}. Even among the studies that did identify participants as having NAFLD, the diagnostic criteria were inconsistent and sometimes inadequate. Scientific associations recommend that for lean NAFLD, other causes of liver disease including lipodystrophy, rare congenital abnormalities, HIV, hepatitis, nutritional and gastrointestinal tract related factors, endocrine disorders, toxin exposures, and medication induced steatohepatitis are considered when making a diagnosis^{3,4,15}. Implementation of these recommendations did not always occur in the research and this potentially contributed to authors drawing inaccurate or inconsistent conclusions about the influence of dietary or physical activity related factors on NAFLD development when other medical conditions were present.

Other shortcomings contributing to the lack of quality in the research included studies not always stratifying data by biological sex, and inadequate racial and ethnic diversity. This was especially apparent during the initial article screening stage of the scoping review where baseline anthropometric measures such as waist circumference were not stratified by biological sex and articles were excluded because it was unclear whether both sexes met the inclusion criteria. It is possible that several articles could have been unnecessarily excluded for this reason. Among the articles that were included in the review, approximately one third of the studies did not stratify data by biological sex and prevented better understanding of any sex differences in etiology of lean NAFLD^{30–32,34,37,40–42,44,48,52,53,64–66,70,74,82,84–86}. It is also necessary to include more diversity in the races or ethnicities represented in the literature to enable more generalizable results. More

ethnic diversity is needed in research to account for biological, genetic, and cultural differences among individuals living in different parts of the world. This is especially important as research indicates that liver fat content differs when comparing Asian groups living in native countries versus in the United States²¹. Additionally, liver fat content and NAFLD prevalence among other ethnic groups in the United States, where higher prevalence of NAFLD was shown in Hispanic individuals and lower prevalence of NAFLD was observed in Black individuals^{91–93}. This suggests that even within a single country, dietary and physical activity risk factors could differ depending on the ethnicity of the population and highlights the overall importance of diverse representation in research.

4.3 Opportunities for Future Research

There are many opportunities for future research on this topic to fill knowledge gaps and improve the overall quality of the evidence. First, research is needed on the current topics that have already been examined in the current body evidence using study designs and methodology that correct for deficits identified in this scoping review. This includes randomized controlled trials and prospective studies, consistent key terminology that has been defined by a consensus in the research community, and clearly indicating the NAFLD status of participants based on a comprehensive diagnostic criterion.

In addition to utilizing higher quality study designs, there are dietary and physical activity related topics that may need to be prioritized in research to enhance understanding of lean NAFLD populations. For example, research is needed to clarify whether recommendations from scientific associations for the prevention and treatment of lean NAFLD are appropriate for lean NAFLD. These recommendations suggest that following a Mediterranean diet, exercising, replacing saturated fat with unsaturated fatty acids, and limiting dietary sources of fructose and

other refined carbohydrates could be beneficial for reducing liver fat in lean individuals^{4,15}. Based on the findings in this scoping review, there is insufficient evidence to support these recommendations due to contradicting results and questionable generalizability to non-Asian populations. Although several studies identified in this scoping review provided consistent evidence to suggest that physical activity was beneficial for reducing NAFLD risk, these studies were primarily based in Asian countries and cannot be generalized to lean NAFLD individuals in non-Asian populations^{10,45,49,53,61,69,77,81,83}. As previously discussed, studies examining the effect of a Mediterranean diet on NAFLD risk provided mixed results and even suggested that there may be no association between Mediterranean diet and NAFLD risk in lean populations^{38,69,75}. Mixed results were also observed when evaluating the effect of saturated fat, unsaturated fats, and refined carbohydrates such as fructose on NAFLD or fatty liver^{10,28,32,36,37,44,62–66,77,81,84}. Research evaluating the association between high fructose beverages such as soda and NAFLD risk were inconsistent ranging from being inversely associated to having no association with NAFLD risk^{59,82,84,85}. However, most studies were based in Asia where soda intake is less common than in non-Asian populations and therefore may not accurately represent the association between soda intake and NAFLD in non-Asian populations⁸². Overall, more research is needed to clarify if recommendations from scientific and professional associations are appropriate for the lean NAFLD population and may need to be tailored to specific ethnicities.

Another topic that should be given priority is alcohol and NAFLD risk in lean individuals. More research is clearly needed to expand the body of evidence to better clarify the true relationship between alcohol intake and NAFLD risk in lean populations. The relationship between alcohol intake and NAFLD (all weight categories) has been controversial due to some research indicating potential protective effects of moderate intake while other research suggests

that there is no safe alcohol intake threshold for NAFLD. However, most of the research is based on studies that involve overweight or obese individuals^{7,24}. Therefore, it is unclear what should be recommended to lean individuals, especially since this scoping review indicated a lack of consensus in the literature where alcohol intake had either positive, negative, or no association with NAFLD risk. The main diagnostic criterion to distinguish NAFLD from AFLD are used to rule out excessive alcohol intake, which is most often defined as < 20 g/day (females) and < 30 g/day (males)^{4,7,15}. More research is needed to clarify whether these alcohol intake thresholds need to be modified for lean populations. Additionally, this scoping review highlighted that some factors such as biological sex, ethnicity, race, and differing levels of leanness may potentially influence the interaction between alcohol intake and NAFLD risk. More high-quality research can clarify whether these interactions do exist, help to tailor NAFLD diagnostic criteria to specific populations, and reduce the incidences of undiagnosed lean NAFLD.

Finally, other topics to prioritize in future research include the application of nutrigenetics to mediate lean NAFLD risk, the influence of microbiome composition, and identifying an ideal macronutrient distribution depending on race or ethnicity. Genetic mutations have been proposed as a key etiological factor for lean NAFLD¹. It has also been used to explain why sometimes lean NAFLD individuals do not significantly differ in dietary or exercise habits from obese NAFLD individuals and yet do not develop obesity and/or other metabolic abnormalities^{1,30,70,84,85}. This scoping review identified only two studies that explored interactions between dietary habits and genetic factors known to be associated with increased NAFLD risk, suggesting a significant knowledge gap on this topic and the need for more research^{48,65}. Similarly, gut dysbiosis has also been a proposed mechanism for the development of lean NAFLD and this scoping review identified only one study on this topic. Researchers

reported a significant difference in microbiome composition in lean individuals with NASH compared to participants without NASH as well as individuals with overweight or obesity and NASH. Because lean NASH participants did not differ in total calorie, macronutrient, or dietary fiber intake compared to the other study groups, the authors concluded that dietary intake did contribute to the differences in microbiome composition observed in lean NAFLD participants. However, the study was limited by a small sample size ($n = 23$) and more research is necessary to better explore whether factors such as diet or physical activity influence microbiome composition in lean NAFLD or NASH individuals³¹. Finally, developing ethnicity-specific macronutrient distributions is another important topic to explore in the future. The potential differences in “ideal” macronutrient distribution based on ethnicity was highlighted by a cross-sectional study in South Korea where U-Shaped figures comparing different levels of macronutrient intake and NAFLD prevalence indicated that 50-60% of calories from carbohydrates and 30-40% of calories from fat would be the most appropriate for the study population⁵⁰. This macronutrient distribution could be considered high when compared to dietary guidelines for Western countries such as the USA or Mexico and thus illustrates the potential need for tailored nutrition recommendations in lean NAFLD^{30,94}.

4.4 Scoping Review Strengths and Limitations

The strengths of this scoping review include the breadth of the research included and the depth of analysis and synthesis of the evidence. By summarizing the available research on the topic of lean NAFLD and dietary and physical activity risk factors, these findings can be a point of reference for future research. One limitation of this scoping review was the use of a broader inclusion criteria for anthropometric measures when selecting articles for eligibility. BMI < 25 kg/m² and WC < 102 cm (males) or < 88 cm (females) were used rather than more ethnicity-

specific criteria especially for Asian populations where research indicates that BMI and WC thresholds for normal weight are lower than for Western countries (most commonly BMI < 23-24 kg/m² and WC < 80-90 cm for both sexes)^{14,26}. However, these lower thresholds for Asian populations were not consistently followed by researchers, and using a higher threshold helped highlight the significant heterogeneity in how researchers define leanness. Additionally, most of the studies using Asian populations had baseline characteristics that met the lower anthropometric parameters for BMI, WC, or both. In the studies where BMI or WC were above the ethnicity-specific parameters, results were often stratified by weight status and/or statistical models were adjusted for BMI or WC^{45,46,53,54,57-60,62,63,67,69,73,76,80-82}. This helped to identify results specifically using individuals with a BMI in alignment with ethnicity-specific parameters, and whether identified risk factors were independent of BMI or WC. Finally, another limitation was the inclusion of studies that measured “fatty liver” without specifying NAFLD, and/or not using a comprehensive exclusion criterion to limit other causes of fatty liver disease such as excess alcohol intake, hepatitis, autoimmune disorders, and drug-induced steatohepatitis. This potentially contributed to inclusion of studies with participants who did not have fatty liver related to NAFLD and incorrect conclusions about certain dietary or physical activity risk factors. It is also possible that studies that did not evaluate alcohol could have included participants with AFLD, though some research suggests that NAFLD and AFLD have overlapping pathologies and patients may often have components of both conditions⁷. Nonetheless, these limitations were considered when evaluating the risks of bias and the validity of results of the included studies.

Chapter 5 - Conclusion

The current scoping review showed the breadth of the available body of evidence, illustrating that a variety of topics have been explored in relation to lean NAFLD risk and protective factors. These factors included the influence of specific diets, food groups, nutrients, beverages, and physical activity. The research was limited by high risk for bias and lack of racial and ethnic diversity among participant samples, as well as significant heterogeneity in results, study methods, and key terms and their definitions. This heterogeneity made it difficult to draw definitive conclusions regarding most dietary and physical activity risk or protective factors for lean NAFLD. Nonetheless, some results indicate potential benefits of diets high in vegetables and low in animal-proteins, sodium, and refined carbohydrates, as well as meeting minimum exercise guidelines of at least 150 minutes of moderate intensity exercise per week. However, these conclusions were based on studies predominantly conducted in Asia and generalizing them to non-Asian populations is not appropriate. Therefore, there are many opportunities for future research including exploring topics on specific diets, food groups, nutrients, beverages, and physical activity patterns using higher-quality study designs, more consistent terminology, diverse populations, and methodologies that better account for the numerous extraneous variables that can influence liver health.

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Appendix A - Additional Reference Tables

Table A.1. Keyword searches for individual databases

PubMed	((("Diet"[MeSH Terms] OR "Diet"[All Fields] OR "diet, healthy"[MeSH Terms] OR "Diet Records"[MeSH Terms] OR "Nutrition Assessment"[MeSH Terms]) AND ("Life Style"[MeSH Terms] OR "Healthy Lifestyle"[MeSH Terms] OR "Risk Factors"[MeSH Terms] OR "risk"[All Fields] OR "Epidemiology"[MeSH Terms] OR "Epidemiology"[All Fields])) AND ("non-alcoholic fatty liver disease"[MeSH Terms] OR "Fatty Liver"[MeSH Terms] OR "nonalcoholic fatty liver disease"[All Fields] OR "nonalcoholic fatty liver"[All Fields] OR "non-alcoholic fatty liver disease"[All Fields] OR "non-alcoholic fatty liver"[All Fields] OR "Fatty Liver"[All Fields] OR "NASH"[All Fields] OR "NAFLD"[All Fields] OR "non-alcoholic steatohepatitis"[All Fields] OR "hepatic steatosis"[All Fields])) AND (("Adult"[MeSH Terms]) AND ("Female"[MeSH Terms] OR "Male"[MeSH Terms])) AND ("Humans"[MeSH Terms])) AND ("Body Mass Index"[MeSH Terms] OR "Body Mass Index"[All Fields] OR "Waist Circumference"[MeSH Terms] OR "thinness/complications"[MeSH Terms] OR "lean"[All Fields] OR "nonobese"[All Fields] OR "non-obese"[All Fields] OR "non-overweight"[All Fields] OR "normal weight"[All Fields] OR "healthy weight"[All Fields]))
Web of Science	(((((TS=(diet or "nutrition assessment" or "diet records" or "healthy diet")) AND TS=("life style" or "healthy lifestyle" or "risk factors" or risk or epidemiology)) AND TS=("non-alcoholic fatty liver disease" or "fatty liver" or "nonalcoholic fatty liver disease" or "nonalcoholic fatty liver" or "non-alcoholic fatty liver" or NAFLD or NASH or "non-alcoholic hepatic steatosis" or "hepatic steatosis")) AND TS=(adult))

	AND TS=(female OR male)) AND TS=(humans)) AND TS=("normal BMI" or "waist circumference" or thinness or "non-obese" or "nonobese" or "lean" or "non-overweight" or "normal weight" or "healthy weight" or "normal body mass index")
Global Health	((((diet or "healthy diet" or "diet records" or "nutrition assessment" or lifestyle or "healthy lifestyle" or "risk factors" or risk or epidemiology) AND ("non-alcoholic fatty liver disease" or "fatty liver" or "nonalcoholic fatty liver disease" or "nonalcoholic fatty liver" or "non-alcoholic fatty liver" or NASH or NAFLD or "non-alcoholic steatohepatitis" or "hepatic steatosis") AND (Adult) AND (Female or male) AND (humans) AND ("body mass index" or "waist circumference" or lean or nonobese or thinness or "non-obese" or "non-overweight" or "normal weight" or "healthy weight"))))
Scopus	(TITLE-ABS-KEY (diet OR "nutrition assessment" OR "diet records" OR "healthy diet") AND TITLE-ABS-KEY ("life style" OR "healthy lifestyle" OR "risk factors" OR risk OR epidemiology) AND TITLE-ABS-KEY ("non-alcoholic fatty liver disease" OR "fatty liver" OR "nonalcoholic fatty liver disease" OR "nonalcoholic fatty liver" OR "non-alcoholic fatty liver" OR nafld OR nash OR "non-alcoholic hepatic steatosis" OR "hepatic steatosis") AND TITLE-ABS-KEY (adults AND (female OR male) AND humans) AND TITLE-ABS-KEY ("normal bmi" OR "waist circumference" OR thinness OR "non-obese" OR "nonobese" OR "lean" OR "non-overweight" OR "normal weight" OR "healthy weight" OR "normal body mass index"))
ProQuest Nursing and Allied Health	((summary(diet OR "nutrition assessment" OR "diet records" OR "healthy diet") AND summary("life style" OR "healthy lifestyle" OR

	"risk factors" OR risk OR epidemiology) AND summary("non-alcoholic fatty liver disease" OR "fatty liver" OR "nonalcoholic fatty liver disease" OR "nonalcoholic fatty liver" OR "non-alcoholic fatty liver" OR NAFLD OR NASH OR "non-alcoholic hepatic steatosis" OR "hepatic steatosis") AND ("normal BMI" OR "waist circumference" OR thinness OR "non-obese" OR "nonobese" OR "lean" OR "non-overweight" OR "normal weight" OR "healthy weight" OR "normal body mass index") AND summary(Adult AND humans AND (female OR male))) OR (title(diet OR "nutrition assessment" OR "diet records" OR "healthy diet") AND title("life style" OR "healthy lifestyle" OR "risk factors" OR risk OR epidemiology) AND title("non-alcoholic fatty liver disease" OR "fatty liver" OR "nonalcoholic fatty liver disease" OR "nonalcoholic fatty liver" OR "non-alcoholic fatty liver" OR NAFLD OR NASH OR "non-alcoholic hepatic steatosis" OR "hepatic steatosis") AND ("normal BMI" OR "waist circumference" OR thinness OR "non-obese" OR "nonobese" OR "lean" OR "non-overweight" OR "normal weight" OR "healthy weight" OR "normal body mass index") AND (Adult AND humans AND (female OR male))) OR (title(diet OR "nutrition assessment" OR "diet records" OR "healthy diet") AND ("life style" OR "healthy lifestyle" OR "risk factors" OR risk OR epidemiology) AND title("non-alcoholic fatty liver disease" OR "fatty liver" OR "nonalcoholic fatty liver disease" OR "nonalcoholic fatty liver" OR "non-alcoholic fatty liver" OR NAFLD OR NASH OR "non-alcoholic hepatic steatosis" OR "hepatic steatosis") AND ("normal BMI" OR "waist circumference" OR thinness OR "non-obese" OR "nonobese" OR "lean" OR "non-overweight" OR "normal weight" OR "healthy weight" OR "normal body mass index") AND (Adult AND humans AND (female OR male))) OR (title(diet OR "nutrition assessment" OR "diet records" OR "healthy diet") AND title("life style" OR "healthy lifestyle" OR "risk factors" OR risk OR epidemiology) AND ("non-alcoholic fatty liver disease" OR "fatty liver" OR "nonalcoholic fatty
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	liver disease" OR "nonalcoholic fatty liver" OR "non-alcoholic fatty liver" OR NAFLD OR NASH OR "non-alcoholic hepatic steatosis" OR "hepatic steatosis") AND ("normal BMI" OR "waist circumference" OR thinness OR "non-obese" OR "nonobese" OR "lean" OR "non-overweight" OR "normal weight" OR "healthy weight" OR "normal body mass index") AND (Adult AND humans AND (female OR male))) OR ((diet OR "nutrition assessment" OR "diet records" OR "healthy diet") AND title("life style" OR "healthy lifestyle" OR "risk factors" OR risk OR epidemiology) AND title("non-alcoholic fatty liver disease" OR "fatty liver" OR "nonalcoholic fatty liver disease" OR "nonalcoholic fatty liver" OR "non-alcoholic fatty liver" OR NAFLD OR NASH OR "non-alcoholic hepatic steatosis" OR "hepatic steatosis") AND ("normal BMI" OR "waist circumference" OR thinness OR "non-obese" OR "nonobese" OR "lean" OR "non-overweight" OR "normal weight" OR "healthy weight" OR "normal body mass index") AND (Adult AND humans AND (female OR male)))) OR (summary(diet OR "nutrition assessment" OR "diet records" OR "healthy diet") AND ("life style" OR "healthy lifestyle" OR "risk factors" OR risk OR epidemiology) AND summary("non-alcoholic fatty liver disease" OR "fatty liver" OR "nonalcoholic fatty liver disease" OR "nonalcoholic fatty liver" OR "non-alcoholic fatty liver" OR NAFLD OR NASH OR "non-alcoholic hepatic steatosis" OR "hepatic steatosis") AND summary("normal BMI" OR "waist circumference" OR thinness OR "non-obese" OR "nonobese" OR "lean" OR "non-overweight" OR "normal weight" OR "healthy weight" OR "normal body mass index") AND (Adult AND humans AND (female OR male))) OR ((diet OR "nutrition assessment" OR "diet records" OR "healthy diet") AND summary("life style" OR "healthy lifestyle" OR "risk factors" OR risk OR epidemiology) AND summary("non-alcoholic fatty liver disease" OR "fatty liver" OR "nonalcoholic fatty liver disease" OR "nonalcoholic fatty liver" OR "non-alcoholic fatty liver" OR NAFLD OR NASH OR "non-alcoholic
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	hepatic steatosis" OR "hepatic steatosis") AND summary("normal BMI" OR "waist circumference" OR thinness OR "non-obese" OR "nonobese" OR "lean" OR "non-overweight" OR "normal weight" OR "healthy weight" OR "normal body mass index") AND (Adult AND humans AND (female OR male)))
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