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# Non-Alcoholic Fatty Liver Disease (NAFLD): A systematic review and meta-analysis based on a lifestyle intervention perspective

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**Abstract**
Non-alcoholic fatty liver disease (NAFLD) is a growing public health concern globally which is estimated around 32.4%.The lifestyle interventions emerging as a primary management strategy which offer potential to mitigate NAFLD and its progression. Thus, this study aimed to evaluate the effect of lifestyle interventions including dietary modifications, physical activity, and weight management in metabolic health indicators associated with NAFLD. Eligible studies meeting the inclusion criteria were considered, evaluated the impact of intervention on anthropometry (BMI, WC), Liver enzymes (ALT, AST, GGT), Lipid Profile and HOMA-IR A random effect meta-analysis was conducted and pooled effect sizes with 95% confidence interval (CI) and heterogeneity ($I^2$) was calculated. Fourteen studies comprising 1494 participants were included in the study. Subgroup analysis revealed that the Mediterranean diet and physical activity (aerobic and resistance training) significantly improved liver enzymes (ALT: SMD= -0.80; AST: SMD= -0.79; $p<0.05$), lipid profiles (TG, LDL, HDL), HOMA-IR (SMD= -0.52, $p<0.05$) and BMI. The combination of dietary and exercise interventions showed greater effectiveness in reducing intrahepatic fat and improving metabolic outcomes than either intervention alone. Though heterogeneity across studies was high ($i^2 > 80$). In conclusion, dietary interventions, especially the Mediterranean diet, combined with aerobic and resistance training, provide the most effective approach for improving liver health and metabolic outcomes in NAFLD. However, individual responses vary, emphasizing the need for personalized treatment plans. Future research should focus on long-term effects to better understand their impact on NAFLD progression and liver health.

**Keywords:** Lifestyle intervention, Mediterranean Diet, Physical Activity, Aerobic exercise, Resistance Training

## Introduction
NAFLD is a spectrum of the disease ranging from non-alcoholic fatty liver (NAFL), which involves simple hepatic steatosis without inflammation, to non-alcoholic steatohepatitis (NASH), characterized by inflammation and hepatocyte injury [1]. It is currently recognized as the most chronic liver disease, and globally affects around 32.4% population and one the most prominent cause of liver related morbidity and mortality [2]. NAFLD is considered a multifactorial disease in which environmental factors, such as nutrient intake and exposure, physical activity, genetics, epigenetics, and gut microbiota composition have been shown to interact with each other contributing to its development [3]. Insulin resistance plays an important role by promoting hepatic de novo lipogenesis (DNL) and glyceroneogenesis, even in non-diabetic individuals leading to increased triglyceride synthesis and hepatic fat accumulation [4]. Dysbiosis of the gut microbiota contributes to increased intestinal permeability, allowing the translocation of bacteria and bacterial endotoxins into the portal circulation, which in turn triggers hepatic inflammation. Additionally, NAFLD susceptibility has been linked to several genetic variants, including PNPLA3 (I148M), TM6SF2 (E167K), and MBOAT7 (rs641738), which are associated with increased hepatic fat storage, inflammation, and fibrosis. Conversely, the HSD17B13 (rs72613567:TA) variant may provide protection against liver inflammation.

These genetic factors affect lipid metabolism, oxidative stress, and inflammatory pathways, contributing to the development and progression of NAFLD. As the disease progresses, fibrosis develops, marked by scar tissue formation in the liver, and can ultimately lead to cirrhosis, wherein the liver becomes extensively scarred, shrunken, and nodular. It is considered as clinical issue, but has now emerged as public health concern due to its association with obesity, insulin resistance, type 2 diabetes mellitus (T2DM), hypertension, hyperlipidaemia, and metabolic syndrome posing a major health and economic burden to all societies. [6] This association primarily driven by high-calorie diet, excess (saturated) fats, refined carbohydrates, sugar-sweetened beverages, a high fructose intake and a Western diet. [7] Although there are no approved pharmacological treatments for NAFLD, several promising agents such as obeticholic acid, aramchol, lanifibranor, and semaglutide are currently under investigation and have shown encouraging results in clinical trials. [8] However, lifestyle modifications, particularly dietary changes and physical activity which can be implemented through public health education, community based intervention and public health programs, remain the primary therapeutic strategies are hypothesized to reduce liver fat content, improve liver enzyme levels, and enhance overall metabolic health (Figure 1). However, it poses challenges due to socioeconomic disparities, long term compliance and cultural habits Despite increasing interest in the non-pharmacological management of NAFLD, few studies have specifically examined the role of the Mediterranean diet, and to date, no meta-analysis has comprehensively evaluated the combined effects of the Mediterranean diet and structured physical activity on insulin resistance and liver enzymes across diverse populations. The sample population consists of adults aged 18 years and older, with comparisons made between different intervention strategies. By pooling data across studies, this analysis seeks to provide a comprehensive understanding of the impact of lifestyle changes on NAFLD progression and to inform metabolic health outcomes for its management. This study addresses that gap by providing a quantitative synthesis of the efficacy of these lifestyle interventions, both individually and in combination.

## Methods

This systematic review was based on the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines [9], PICOC framework was used (Table 1). Zotereo was used to gather, store and organize the references, including the elimination of duplicates. [10] The protocol was prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO; Registration No: CRD420251105670, available from: https://www.crd.york.ac.uk/PROSPERO/view/CRD420251105670).

### Systematic Search

Searches were performed in English language with filters for adult populations and study types such as RCTs in database such as Google Scholar, EMBASE, EBSCO and PubMed. Keywords were "Non-alcoholic Fatty Liver Disease"[MeSH] OR "non-alcoholic fatty liver disease" OR "NAFLD" OR "hepatic steatosis" OR "fatty liver" OR "non-alcoholic steatohepatitis" OR "NASH", "Diet Therapy"[MeSH] OR "dietary intervention" OR "Mediterranean diet" OR "low-calorie diet" OR "nutrition therapy" OR "diet" OR "lifestyle modification", "Exercise Therapy"[MeSH] OR "physical activity" OR "aerobic exercise" OR "resistance training" OR "moderate exercise" OR "sedentary behaviour" OR "combined lifestyle intervention", "Insulin Resistance"[MeSH] OR "insulin resistance" OR "HOMA-IR"

AND "Liver Enzymes" [MeSH] OR "ALT" OR "AST" OR "GGT" OR "liver enzymes"

### Study Selection and eligibility criteria

- **Inclusion criteria:** Studies included in present meta-analysis were those which used standardized techniques, including imaging or biopsy, to diagnose adults with non-alcoholic fatty liver disease (NAFLD) in order to assure diagnostic consistency. Eligible studies included measurement of pertinent outcomes like liver fat content, liver enzymes, or metabolic parameters and evaluate lifestyle interventions like dietary changes, physical exercise, or combination approaches.
- **Exclusion criteria**: Studies involving non-adult populations, *in vitro* research, animal research, secondary causes of liver disease, such as alcohol-related liver disease, and interventions that don't primarily focus on lifestyle (like pharmaceutical therapies) were typically left out. Studies where the full text was unavailable in English were excluded. To ensure data quality and relevance, studies with insufficient data or without a specified follow-up duration or NAFLD-specific outcome measures were excluded.
- **Outcome measure:** Hepatic fat content or steatosis grade, blood pressure, insulin resistance (HOMA-IR), lipid profiles (total cholesterol, LDL, HDL, and triglycerides), anthropometric factors (BMI, waist circumference), and liver enzymes (ALT, AST, and GGT) were among the outcome measures. These indicators were selected due to their proven significance in the diagnosis, development, and related metabolic dysfunction of NAFLD. Elevated liver enzymes (ALT, AST, and GGT) represent liver damage, Anthropometry measurement (BMI & WC) central obesity or fat accumulation which is hallmark for the progression of NAFLD. Triglycerides and Blood Pressure coexist with NAFLD which also lead to cardiovascular risk. HOMA-IR is measure of insulin resistance, encapsulates a key pathogenic mechanism in the onset and progression of NAFLD.

### Data Extraction

Two reviewers independently evaluated articles for eligibility based on titles and abstracts. Full-text articles were assessed for final inclusion, with exclusion reasons documented. We gathered the following data from every paper, study design (randomized controlled trial) country, year of publication, and author name. The demographics of the population included baseline health problems such type 2 diabetes or obesity, age, sex distribution, and sample size. The Fatty Liver Index (FLI),) and imaging (ultrasound, Fibro Scan, MRI) were among the diagnostic methods used to confirm NAFLD. Type (e.g., Mediterranean diet, aerobic or resistance exercise), dietary components (e.g., olive oil, whole grains), exercise protocols (e.g., type, frequency, and intensity), information about the comparator/control group, and the length of the intervention (ranging from 8 weeks to 18 months) were all detailed in the documentation.

**Data synthesis and analysis**

To quantitatively evaluate the effects of dietary, physical activity, and combined lifestyle interventions on NAFLD-related parameters, a meta-analysis was conducted using standardized statistical methods. The standardized mean difference (SMD) with 95% confidence intervals (CIs) was used to measure the impact of interventions on liver enzymes (ALT, AST, and GGT), anthropometric parameters (BMI, WC), lipid profile (TC, TG, LDL, HDL), and insulin resistance (HOMA-IR), with statistical significance set at $p<0.05$. Heterogeneity among studies was assessed using Cochran's $Q$ test and quantified with the $I^2$ statistic, where high heterogeneity ($I^2 > 75\%$) prompted subgroup analyses to identify potential influencing factors. Subgroup analyses were performed based on intervention type (diet, physical activity, or combined), study duration, and population characteristics (e.g., obesity, diabetes, metabolic syndrome The meta-analysis was performed using Review Manager 5.4.1[11] and Meta-Analysis Online [12], which facilitated data consolidation, Risk bias assessment, forest plotting, heterogeneity testing, and subgroup analysis, with results visually represented through forest plots to illustrate overall effect sizes and individual study contributions.

**Results**

**Literature search result and study selection process**

As shown in the PRISMA flow diagram (Figure 2), 3,400 records were identified through database searches. After removing duplicates (N=2,307), 246 records were screened, with 232 excluded for the following reasons: Non-Randomized studies (N=50), Intervention did not inclusion (N=47), Animal or *in vitro* studies (N=50), Studies on children and adolescents (N=14), Conference (N=15), Studies outside the scope (15), other language (N=21), only Abstract (N=20). Fourteen studies were included, focusing on NAFLD in populations with overweight/obesity or diabetes. Randomized clinical trial studies were selected (N=14). (Figure 1). These were classified into three categories: Dietary interventions (Mediterranean diet), physical activity interventions, and combined diet and exercise interventions.

**Characteristics of included trials**

In total, fourteen RCT were reviewed encompassing 1494 participants across various countries Italy, Australia, China, Iran, Saudi Arabia, Israel, London, Greece, Spain and Serbia. The included studies were published between2014 to 2022 and intervention duration between 8 weeks to 18 months. Intervention included in this studied are Mediterranean diet, Olive oil based dietary pattern, Physical activity (aerobic and resistance training) and combined intervention.

**Risk of bias assessment**

Risk of bias was assessed using the Cochrane tool and is summarized in Figure 3. Most studies showed a low risk in domains such as incomplete outcome data, selective reporting, and other biases. However, allocation concealment and blinding of participants and personnel frequently had a high risk of bias**,** likely due to the nature of the interventions. Variability was observed in blinding of outcome assessment. These findings highlight potential performance and selection bias**,** which may influence the overall results.

**Impact Analysis of Mediterranean diet intervention on NAFLD and other parameters**

This meta-analysis indicates that the Mediterranean diet exerts a moderate-to-large effect on NAFLD and other parameters with a standardized mean difference (SMD) of -0.797 (95% CI: -1.385 to -0.208, P=0.01022), signifying a statistically significant improvement in hepatic health [13-16]. Across the included studies, dietary interventions, particularly the Mediterranean diet, demonstrated varying effects on anthropometric measures such as body mass index (BMI), waist circumference (WC), and waist-hip ratio (WHR). [13, 14, 16]. Several studies reported significant reductions in BMI, WC, and WHR following Mediterranean diet interventions, especially when combined with calorie restriction or individualized dietary counselling [13, 16]. However, some studies observed non-significant changes in BMI and WC, suggesting variation in effectiveness [14, 16]. In terms of liver enzyme levels, dietary interventions were associated with consistent and significant improvements. [13-16] Notably, ALT and AST levels showed marked reductions in participants following Mediterranean, whole-grain-enriched, or olive oil-based diets. [13-16] In some studies, GGT also decreased significantly [13,15], while others reported minimal or no change, [14, 16] indicating mixed effects. One study quantified the reductions with an SMD of -0.5 to -0.9 for ALT and AST, and -0.4 for GGT, while another observed reduction in AST of nearly -1.5 SMD [13, 16]. These changes are clinically meaningful, as elevated transaminases are common markers of hepatic inflammation and fat accumulation in NAFLD. Additionally, improvements in liver enzymes often coincided with reductions in liver steatosis grade, further supporting the therapeutic role of diet. [15] Meta-analytic results supported these findings, revealing significant pooled effects on ALT ($I^2=92\%$, $p<0.001$) and AST ($I^2=88\%$, $p<0.001$), while the effects on GGT were inconsistent ($I^2=19\%$, P=0.29). Improvements in lipid profiles were also noted, with several interventions leading to reductions in total cholesterol (TC), triglycerides (TG), and low-density lipoprotein (LDL) cholesterol, alongside increases in high-density lipoprotein (HDL). [13, 15] Yet, other trials reported no significant changes in lipid levels, highlighting the variability in response.[14, 16] The impact on insulin resistance, measured by HOMA-IR, also varied; some studies documented significant improvements following Mediterranean or low-fat diet interventions, while others showed non-significant changes, particularly in those following whole grain or olive oil-enriched diets [13-15]. Regarding blood pressure, the Mediterranean diet did not show a significant pooled effect on either systolic (SMD: 0.08 [-0.24, 0.41]) or diastolic BP (SMD: -0.07 [-0.83, 0.69]), with most individual studies reporting non-significant changes, except for one that noted a modest diastolic reduction [13, 15]. (Table 2) High heterogeneity ($I^2 > 90\%$) observed across many analyses is likely due to variations in Mediterranean diet composition (e.g., use of olive oil, whole grains, or calorie restriction), dietary adherence, intervention duration, and participant characteristics such as age, BMI, and comorbidities [13-16].

Differences in adjunct therapies and outcome measurement techniques may also have contributed to this variability (Figure 4).

**Impact analysis of physical activity on NAFLD and other parameters**

This meta-analysis demonstrates that physical activity has a statistically significant impact on NAFLD-related outcomes, with a standardized mean difference (SMD) of -0.80 (95% CI: -1.385 to -0.208, P=0.01022) [17-21]. Exercise interventions were consistently associated with improvements in anthropometric parameters, liver enzyme profiles, lipid metabolism, and insulin sensitivity [17, 19-21]. Structured physical activity including aerobic exercise, resistance training, and high-intensity interval training led to reductions in body weight (BW), body mass index (BMI), and waist circumference (WC) [17, 19, 20]. Resistance training appeared slightly more effective for BMI and weight reduction, although both aerobic and resistance modalities demonstrated comparable efficacy in reducing central adiposity [18-20]. In all intervention groups, significant reductions in WC and BMI were more common than in controls, where no notable changes were observed, emphasizing the role of exercise in targeting abdominal fat and overall obesity in NAFLD patients [17-21]. Exercise also showed favourable effects on liver enzymes. Several trials reported significant reductions in alanine aminotransferase (ALT) and aspartate aminotransferase (AST) following aerobic or resistance training, with some also demonstrating decreases in gamma-glutamyl transferase (GGT) [17, 19-21]. These improvements often corresponded with reductions in hepatic fat content, suggesting enhanced liver function and reduced steatosis [18-20]. However, in some studies, changes in liver enzymes did not reach statistical significance, indicating variability in individual responses or intervention intensity [17, 18]. Regarding blood pressure, both aerobic and moderate-intensity exercise interventions were associated with significant reductions in systolic and diastolic BP, particularly in participants with central obesity or comorbid diabetes [17-19]. These findings underline the cardio metabolic benefits of physical activity in NAFLD management, extending beyond liver-specific outcomes. Lipid profile outcomes varied however several studies reported significant reductions in total cholesterol, triglycerides, and LDL cholesterol, along with increases in HDL cholesterol, [18, 20, 21] other trials found no substantial differences, particularly with moderate-intensity exercise [17]. Resistance training was more consistently associated with improvements in triglyceride and HDL levels, [18, 20] while aerobic and high-intensity interventions also showed potential benefits [17, 18]. These outcomes suggest a modality- and intensity-dependent effect of physical activity on lipid metabolism. The influence of exercise on insulin resistance, as measured by HOMA-IR, was mixed. Some interventions, particularly those involving high-intensity interval training or aerobic protocols, reported significant reductions in HOMA-IR values [18, 20]. In contrast, other studies did not observe statistically meaningful improvements despite favourable changes in anthropometric and hepatic outcomes. [17, 19, 21] (Table 3). This inconsistency may reflect differences in baseline metabolic status, duration of intervention, or adherence levels. A high level of heterogeneity was detected across studies ($I^2$=94%, $p$<0.01), indicating substantial variability in effect size and direction. This heterogeneity is likely attributed to variations in exercise type (aerobic, resistance, high-intensity), intervention duration, participant characteristics (e.g., presence of diabetes, obesity), adherence rates, and differences in outcome assessment methods, such as liver enzyme assays and HOMA-IR calculations [17-21]. These methodological and clinical differences may limit the generalizability of pooled findings and highlight the need for standardized protocols in future trials (Figure 5).

**Impact analysis of combined intervention involving both Mediterranean diet and physical activity on NAFLD and other parameters**

Combined Mediterranean diet and physical activity interventions have demonstrated significant and clinically relevant benefits across multiple NAFLD-related outcomes. Meta-analysis revealed a pooled standardized mean difference (SMD) of -0.616 (95% CI: -1.134 to -0.118, $p$<0.05), reflecting consistent improvements in anthropometric, hepatic, lipid, and glycaemic parameters. [22-26]Across the included studies, notable reductions in body weight (BW), body mass index (BMI), and waist circumference (WC) were observed. [24, 25, 28] For instance, Mediterranean diet protocols with high meal frequency (MD-HMF) resulted in greater reductions in BMI and WC compared to traditional diets. [23] Additional reductions were reported when the Mediterranean diet was combined with moderate-to-vigorous exercise, aerobic or resistance training, or accompanied by adequate sleep. [22-24] Overweight NAFLD patients receiving these combined interventions consistently showed improved BW and WC outcomes. Furthermore, both the conventional Mediterranean diet and polyphenol-rich Green-MED (supplemented with Mankai strain and green tea) resulted in marked reductions in BMI and WC, highlighting the additive benefit of bioactive-rich foods when paired with structured physical activity [26].

Significant improvements in liver enzyme levels were also reported. In one study, ALT levels were reduced with an SMD of -1.43 (95% CI: -2.19 to -0.66), while GGT was reduced with an SMD of -0.20 (95% CI: -0.88 to 0.45). [22] Other studies demonstrated consistent decreases in ALT and AST levels, often exceeding the reductions observed with di*et al*one. [23, 25, 26] These enzymatic improvements were frequently associated with reductions in hepatic fat content, suggesting enhanced liver function and reduced steatosis. [24, 26] Blood pressure also improved across several interventions, particularly those combining diet with physical activity. [22, 24, 26] For example, diastolic BP significantly decreased in the Mediterranean diet group compared to low-fat diets, while Green-MED interventions led to overall BP reduction in overweight and dyslipidemic individuals. [24, 26] These findings underscore the cardiovascular and metabolic benefits of lifestyle changes in NAFLD management. Additionally, positive effects on lipid profiles were consistently reported, including significant reductions in total cholesterol (TC), triglycerides (TG), and low-density lipoprotein cholesterol (LDL), alongside increases in high-density lipoprotein cholesterol (HDL) [22-25]. Some interventions reported both lipid improvements and transaminase reductions within the same cohorts, supporting the broad metabolic impact of these lifestyle modifications [25, 26].

Insulin resistance, assessed using the homeostatic model assessment (HOMA-IR), improved significantly in most studies. Reductions in HOMA-IR ranged from an SMD of -0.12 (95% CI: -0.56 to 0.79) to -0.52 (95% CI: -0.92 to -0.13), with greater effects noted in interventions combining dietary strategies with structured physical activity. [22, 25, 26] These reductions were particularly evident in overweight NAFLD patients and in those receiving the Green-MED or conventional Mediterranean diet coupled with exercise. [24, 26] Despite the overall positive findings, a high level of statistical heterogeneity was observed ($I^2$=81%), suggesting substantial variability across studies (Table 4). This heterogeneity is likely due to differences in dietary protocols (e.g., standard vs. polyphenol-enriched diets), exercise modalities (aerobic, resistance, or combined), intervention duration, participant characteristics (such as BMI, comorbid diabetes), and the methods used to assess outcomes (e.g., HOMA-IR, liver enzyme assays). Additional variation may stem from differences in adherence rates, study design, and meal timing strategies. These factors may limit the generalizability of the pooled results; however, the consistency of favourable outcomes across diverse interventions supports the use of combined Mediterranean dietary and physical activity strategies as a robust non-pharmacological approach to NAFLD management (Fig 6).

## Discussion

The present meta-analysis demonstrates that adherence to the Mediterranean diet (MD) is associated with significant improvements in hepatic parameters, including reductions in liver stiffness, steatosis grade, and key liver enzymes (ALT, AST, GGT), as well as favourable changes in lipid profiles, specifically triglycerides (TG) and low-density lipoprotein cholesterol (LDL-C). Additionally significant improvements were observed in insulin resistance (HOMA-IR) and systolic blood pressure. However, the effects on anthropometric measures such as body mass index (BMI), waist circumference, and body weight were inconsistent, suggesting that the MD may exert more pronounced effects on liver-specific and metabolic outcomes than on general anthropometric indices. These findings are consistent with previous evidence from systematic reviews and meta-analyses, which reported significant reductions in Fatty Liver Index (FLI), ALT levels, and liver stiffness following MD interventions, but no significant changes in AST, hepatic steatosis, or BMI. [27] Similar results were reported in another review, which noted significant reductions in liver stiffness and total cholesterol (TC), yet no meaningful improvements in waist circumference or hepatic enzymes such as ALT and GGT. [28] This indicates that the MD may predominantly influence hepatic stiffness and lipid parameters, with variable effects on enzyme levels. Conversely, a meta-analysis and meta-regression involving six randomized controlled trials (RCTs) reported no significant improvement in waist circumference, BMI, liver stiffness, or ALT levels [29]. Nevertheless, notable reductions in FLI (SMD: -1.06; 95% CI: -1.95 to -0.17) and HOMA-IR (SMD: -0.34; 95% CI: -0.65 to -0.03) were observed, highlighting potential benefits of the MD in reducing hepatic fat accumulation and enhancing insulin sensitivity, even in the absence of substantial changes in anthropometric or enzymatic markers. A cross-sectional cohort study further demonstrated an inverse association between MD adherence and the risk of hepatic fibrosis in individuals with NAFLD, [30] reinforcing its hepatoprotective role.

An RCT evaluating a combined intervention of aerobic exercise and a low-glycaemic index Mediterranean diet (LGIMD) reported the greatest reduction in controlled attenuation parameter (CAP), a surrogate marker for hepatic steatosis, particularly among patients with severe NAFLD [31]. Improvements in HOMA-IR were also noted, underscoring the synergistic benefits of dietary and physical activity modifications. Differences in outcomes across studies may be attributable to variability in exercise modality, intensity, and dietary composition (e.g., Green-MED vs. traditional MD), thus limiting the generalizability of findings. Consistent with previous literature, our findings support the role of physical activity, particularly aerobic training, in improving liver enzymes and insulin sensitivity in NAFLD patients. Moreover, when lipid profile optimization is a therapeutic goal, a combination of aerobic and resistance training appears to yield superior outcomes [32]. While aerobic training alone was most effective in improving ALT and HDL-C levels, resistance training had a greater effect on AST reduction. Another RCT comparing moderate-intensity aerobic versus resistance exercise, combined with dietary interventions, found both modalities led to significant reductions in hepatic fat and waist circumference and improved insulin sensitivity, albeit without significant changes in liver enzyme levels or body composition over a 12-week period [33]. It is important to note that not all metabolic markers were assessed in every included study, which may influence the overall interpretation of specific outcomes such as BMI, TG, AST, ALT, GGT, HOMA-IR, and blood pressure.

## Strength and Limitations

It is one of the few studies that systematically assesses how the Mediterranean diet and structured exercise together affect important outcomes linked to non-alcoholic fatty liver disease (NAFLD), such as lipid profiles, insulin resistance, and liver enzymes. The comprehensiveness of the literature search was improved by using both MeSH and non-MeSH terms across several databases. Two reviewers independently carried out the data extraction process, and standardized techniques were applied to the outcome synthesis. Due to the search being limited to English-speaking publications, language bias may have been introduced. There was a notable degree of heterogeneity across the included studies, which was probably caused by differences in follow-up periods, population characteristics, outcome assessments, and intervention methods. Because most trials had relatively short intervention durations, it was difficult to evaluate long-term impacts. The possible differences in outcome measuring techniques between researches represent another drawback. The observed heterogeneity in pooled results may be caused by variations in anthropometric assessment procedures, laboratory testing for liver enzymes, or HOMA-IR calculation techniques, for example. It is important to take these methodological differences into account when interpreting the results.

## Future Directions

To enhance the current evidence base, future investigations should prioritize rigorously designed randomized controlled trials employing standardized intervention protocols and extended follow-up periods. Particular emphasis should be placed on evaluating the long-term effects of combined dietary and physical activity interventions on clinically meaningful outcomes, including liver fibrosis and liver-related morbidity. Moreover, future studies should address real-world implementation challenges, such as patient adherence, cultural dietary patterns, and socioeconomic determinants of lifestyle modification. Mechanistic research examining the roles of gut microbiota, systemic inflammation, and genetic predisposition may yield valuable insights into the biological pathways through which lifestyle interventions exert their effects on NAFLD progression. Finally, the development of individualized treatment strategies tailored to demographic and clinical characteristics such as age, sex, metabolic status, and comorbidities will be essential for optimizing the efficacy and translational potential of lifestyle-based therapeutic approaches.

## Conclusion

The combination of dietary interventions, particularly the Mediterranean diet, and physical activity, particularly aerobic and resistance training, offers the most comprehensive approach to improving liver health and metabolic outcomes in NAFLD patients. However, individual variations in response to these interventions highlight the need for personalized treatment plans that account for specific patient characteristics and clinical conditions. Future studies should continue to explore the effects of these interventions, especially with longer follow-up periods, to better understand their long-term impact on NAFLD progression and liver health.

## List of Abbreviations

- ALT=Alanine aminotransferase
- AST=Aspartate aminotransferase
- BMI=Body mass index
- BP=Blood pressure
- BW=Body weight
- CAP=Controlled attenuation parameter
- CI=Confidence interval
- FBS=Fasting blood sugar
- FLI=Fatty liver index
- GGT=Gamma-glutamyl transferase
- HbA1c=Glycated hemoglobin
- HDL=High-density lipoprotein
- HFC=Hepatic fat content
- HOMA-IR=Homeostasis model assessment of insulin resistance
- HS=Hepatic steatosis
- IHF=Intrahepatic fat
- IHTG=Intrahepatic triglyceride
- IQR=Interquartile range
- LDL=Low-density lipoprotein
- LFD=Low-fat diet
- LSM=Liver stiffness measurement
- MD=Mediterranean diet
- MUFA=Monounsaturated fatty acid
- NAFL=Non-alcoholic fatty liver
- NAFLD=Non-alcoholic fatty liver disease
- NASH=Non-alcoholic steatohepatitis
- NS=Non-significant
- OR=Odds ratio
- PROSPERO=International Prospective Register of Systematic Reviews
- RCT=Randomized controlled trial
- SD=Standard deviation
- SMD=Standardized mean difference
- TC=Total cholesterol
- TG=Triglycerides
- WC=Waist circumference
- WHR=Waist-to-hip ratio

**Table 1:** PICOC Framework

| Element | Details |
|---|---|
| Population | NAFLD in adults (≥ 18 years old) who have been diagnosed by imaging, liver biopsy, or biomarkers. |
| Intervention | Lifestyle changes include physical activity (aerobic, resistance, or mixed exercise) and/or dietary modifications (e.g., the Mediterranean diet and its components). |
| Comparator | Usual care, no intervention, or alternative interventions |
| Outcome | Improvement in liver health and metabolic parameters |
| Context | Settings such as clinical trials. |

**Table 2:** Study characteristics evaluating mediterranean diet interventions for NAFLD

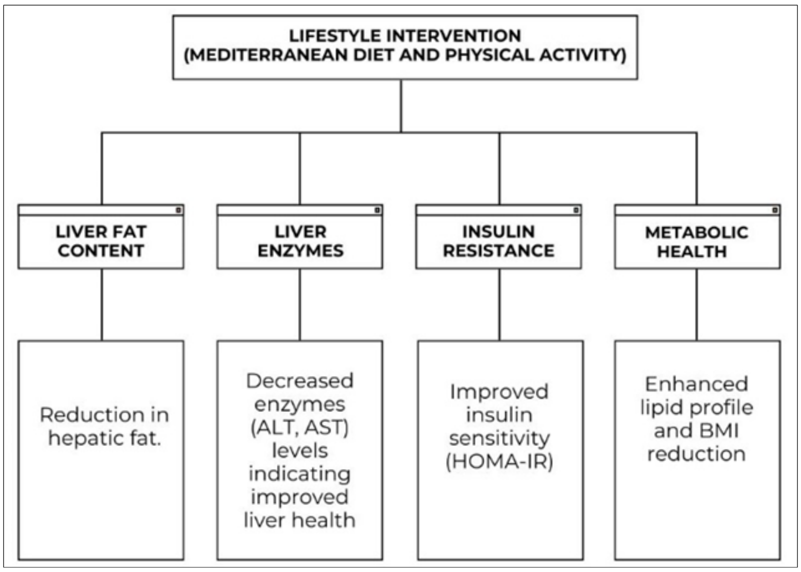
| References | Study Characteristics | Intervention & Comparator/Control | Outcomes measure | Result |
|---|---|---|---|---|
| Abenavoli *et al*., 2017 [13] (Italy) | Study Type: Randomised Controlled trial<br>N=50 participants<br>Duration: 6 months<br>Diagnosis: Ultrasound | Mediterranean diet<br>Group A (N=20) and B (N=20): Calorie Restriction: 1400-1600kcal/day<br>Group B also received two pills of BIL complex daily<br>Group C (Control), (N=10): No treatment | BMI, WC, WHR, BP FLI, LDL, HDL, TG, TC, AST, ALT, GGT, HOMA-IR | ↓ BMI, WHR, TG, GGT, TC, LDL, FLI Significant in Group A and Group B.<br>↓ BP (systolic), WC, ALT, fasting glucose, HOMA-IR Significant in Group B<br>Significant improvements in blood markers in Group C |
| George *et al*., 2022 [14] (Australia) | Study Type: Randomised Controlled trial<br>N=42 participants<br>Duration: 3 months<br>Diagnosis: Ultrasound or Liver Biopsy | Intervention: Mediterranean diet (N=19) (44% of energy from fat (>50% MUFA), 33% from CHO, 15%-20% from protein and up to 5% from alcohol,<br>vs. Low Fat Diet (N=23) (30% fat, 50% carbohydrate and 20% protein) | BMI, WC, IHL, HOMA-IR, LSM, AST, ALT, GGT | ↓ IHL in LFD group (Significant) and (NS) ↓ in Med Diet group<br>↓ Hepatic steatosis and HOMA-IR Significant in LFD group<br>↓BMI and WC (NS) in both group<br>↓AST, ALT and GGT (NS) |
| Dorosoti, 2020 [15] (Iran) | Study Type: Randomised Controlled trial<br>N=112 participants<br>Duration: 3 months<br>Diagnosis: Ultrasound | Intervention: (N=56)<br>Increased whole grain 1/2 of the serving (MD component)<br>Control: (N=56) Standard diet (usual cereals) | AST, ALT, GGT, LS (Liver steatosis grade) BMI, WHR, BP TC,TAG, HDL, LDL, FBS, HOMA-IR | ↓ Liver Steatosis grade (Significant), ALT, AST, GGT<br>↓ BP (Systolic and Diastolic), TC, LDL (Significant).<br>↓ TAG, HDL, FBS, HOMA-IR, BMI, WHR (NS) |
| Shidfar, 2018 [16] (Iran) | Study Type: Randomised Controlled trial<br>N=50 participants<br>Duration: 3 months<br>Diagnosis: Ultrasound | Baseline: Both group 50% CHO, 20% protein and 30% fat<br>Intervention(Olive oil group): Increased Olive oil intake (20% of total fat)<br>Control group: Standard diet | BMI, WC, ALT, AST, HS | ↓ HS and AST (intervention)<br>↓ (Significant) ALT and AST (intervention vs. control)<br>↓ (NS) WC and BW (both) |

**Table 3:** Study characteristics evaluating physical activity interventions for NAFLD

| References | Study Characteristics | Intervention & Comparator/Control | Outcomes measure | Result |
|---|---|---|---|---|
| Zhang *et al.*, 2016 [17] (China) | **Study type:** Randomised Controlled trial N=220 participants<br>Duration: 6months and 12 months<br>Ultrasound and MRI | Aerobic training (N=73)<br>Vigorous-Moderate exercise session (jogging 150min/week) and brisk walking for 6 months<br>Moderate exercise (N=73): Brisk walking 150min/week for 12 months<br>Control group (N=74) | TG, BMI WC, BP, ALT,AST, GGT, IHTG | ↓IHTG (NS) (aerobic and moderate group)<br>↓ (Significant) BP (Systolic and Diastolic) (aerobic and moderate group)<br>↓ (Significant) BW and WC (aerobic and moderate group)<br>↓ lipid level (NS)<br>↓ ALT and GGT (NS)<br>↑ AST significantly |
| Abdelbasset *al.*, 2020 [18] (Saudi Arabia) | **Study type:** Randomised Controlled trial N=47 participants<br>Duration: 8 weeks<br>Diagnosis: MRI | Group 1 (N=16): HII exercise 3 times/ week for 8 weeks (HII group) with medical treatment<br>Group 2 (N=15): Received moderate-intensity continuous (MIC) exercise 3 times/ week for 8 weeks (MIC group)<br>Group 3 (N=16): Control group (only medical treatment) | IHTG, BMI, TG, HDL, HOMA-IR, ALT | ↓ Significant in HFC BMI, IHTG, ALT and lipid profile. But (NS) difference found between HII group and MIC group |
| Zelber Sagi *et al.*, 2014 [19] (Israel) | **Study type:** Randomised Controlled trial N=82 participants<br>Duration: 6 month<br>Diagnosis: Ultrasound | Resistance training (N=44) : 3*3 times/week-8-12 repetition<br>Control arm (N=38) | BMI, WC, BP, HbA1c, HDL, TG, FBG,HFC | ↓ HFC, BMI and WC in resistance training group |
| Shamsoddini *et al.*, 2015 [20] (Iran) | **Study Type:** Randomised Controlled trial N=30 participants<br>Duration: 8 weeks<br>Diagnosis: Ultrasound | Aerobic exercise (running on treadmill 45 min session 3 times/week)<br>Resistance training (seven exercises 45 min session 3 times/week)<br>Control group (no exercise training programme) | BMI, WHR, AST, ALT, Liver steatosis grade, HOMA-IR | ↓ BW and BMI (Significant in resistance training<br>Basal fatty liver reduced in aerobic and resistance training<br>↓ALT, AST, and hepatic fat in aerobic and resistance groups vs. control (Significant)<br>↓ HOMA-IR (aerobic vs. control) (Significant) |
| Shoajee Moradie *et al.*, 2016 [21] (London) | **Study type:** Randomised Controlled trial N=27 participants<br>Duration: 16 weeks<br>Diagnosis: Ultrasound or Liver biopsy | Exercise group (N=15): Moderate intensity workout for 20 minutes/4-5 /week<br>Control group (N=12) : No exercise | BW, BMI, WC AST, ALT, GGT, TG, LDL, TC | ↓ BW, WC, BMI (NS) in exercise group with no change in control group<br>↓ AST and GGT (Significant) in exercise group<br>↓ ALT (both)<br>↓ LDL (Significant) in exercise group |

**Table 4:** Study Characteristics Evaluating Combined Interventions (Mediterranean diet and Physical Activity) for NAFLD

| References | Study Characteristics | Intervention & Comparator/Control | Outcomes measure | Result |
|---|---|---|---|---|
| Kastsagoni *et al.*, 2018 [22] (Greece) | Study type: Randomised Controlled trial<br>N=63 participants<br>Duration:6 month<br>Diagnosis: Ultrasound | Intervention<br>group (N=21) (Healthy lifestyle diet)<br>B: Med Diet Group (N=21) (Intensive counselling programme (60min)<br>C: Med Lifestyle Group (N=21) (Intensive counselling programme (60min)<br>Moderate-vigorous intensity 30 min/d, optimal sleep duration (i.e. ≥7 and ≤ 9 h/d) | BMI, TC, TAG, HDL, LDL,ALT, AST, GGT, BP, HOMA-IR, LSM, NFS | ↓LSM (intervention (MDG and MLG) vs. control)<br>↓ALT (Intervention (MLG) vs. control)<br>↓LDL and Non-HDL (intervention(MDG)<br>↓Median BW (intervention vs. control) |
| Montemayor *et al.*, 2022 [23] (Spain) | Study type: Randomised Controlled trial<br>N=155 participants<br>Duration: 6 months and 12 months<br>Diagnosis: MRI | Conventional Diet (CD) AASLD recommendation (N=51) (25-30% fat, 10-35% protein, 45-65% CHO, 25% fibre, <250mg/d cholesterol and 10,000 steps a day)<br>Mediterranean diet-High Meal Frequency (MD-HMF) (N=52) (30-35% MUFA, 25% protein (vegetable source), 40-45% CHO, (50-70% total CHO (low glycemic index), 10,000 steps a day)<br>Mediterranean diet-Physical activity (MD-PA) (N=52) (35-40% fat 20% proteins and 40-45% or more of total calories from CHO (low glycemic index). Sodium < 6 g a day (2.4 g of sodium), and dietary fibre 30-35 g/day, 35 min interval training session 3 times/week) | BMI, WC, BP FBS, IHF<br>HbA1C, AST, GGT, ALT, GGT, TC, TG, LDL | ↓ Biochemical lipid markers.<br>Improvement in BMI and WC in MD-HMF group<br>↓ IHF (all intervention groups without Significant difference)<br>↓ liver Enzymes (NS ) |
| Gepner *et al.*, 2018 [24] (Israel) | Study type: Randomised Controlled trial<br>N=298 participants<br>Duration:6 months<br>Diagnosis: MRI | Intervention: MD (N=139)<br><40g CHO then < 70g polyphenol rich product<br>Comparator: low fat diet (N=139) 30% of calories, with ≤10% of saturated fat and ≤ 300 mg of cholesterol/ day, and to increase dietary fibre.<br>Physical activity: Aerobic/ resistance training 3d/week | HS, BW, WC, TG, BP, HDL, HOMA-IR, | ↓TG, diastolic BP and [ HDL (intervention vs. comparator)<br>↓BW (both)<br>↓WC (intervention vs. comparator)<br>↓HS (intervention vs. comparator) |
| Ristic-Medic *et al.*, 2021 [25] (Serbia) | Study type: Randomised Controlled trial<br>N=24 participants<br>Duration:3 months<br>Diagnosis: Ultrasound | Intervention: MD 50% CHO, 15% PRO and >30%.<br>Comparator: Low-fat/high CHO 60% CHO, 15% PRO and<br>Physical activity: 30min | BMI, WC, ALT, AST, GGT, TG, TC, HDL, LDL, HOMA-IR | ↑ HDL<br>↓ALT, AST,GGT, TG, TC, LDL, HOMA-IR, BW, WC (both) |
| Meir *et al.*, 2021 [26] (Israel) | Study type: Randomised Controlled trial<br>N=294 participants<br>Duration: 18 months<br>Diagnosis: MRI | Intervention groups: Healthy dietary guidelines (HDG), MED (Rich in vegetables, poultry and fish, 28g/d walnut), Green-MED (3-4 cups/day of green tea and 100 g/day of frozen Mankai strain), all combined with physical activity (PA) (45-60 min/ 3-4 times/week) | IHF, BMI, WC, BP, TC, HDL, LDL, TG, HOMA-IR, AST, ALT | ↓ IHF in Green MED group (Significant)<br>↓BMI and WC (MED group and Green MED group)<br>↓AST and ALT<br>(Green MED group) |




**Source:** Authors own work

**Fig 1:** Impact of lifestyle interventions on key NAFLD Parameters

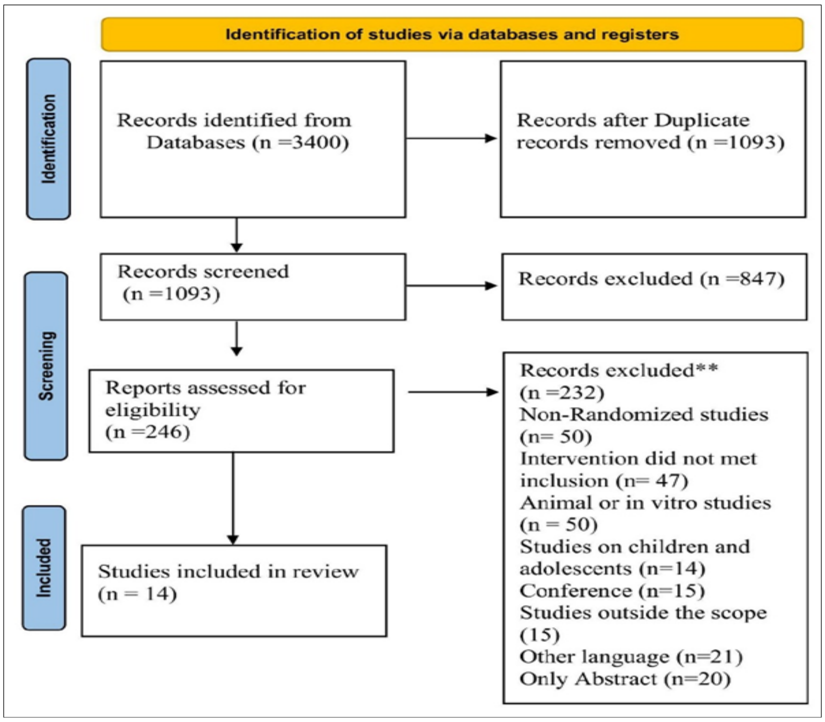



**Fig 2:** PRISMA Framework for the study selection process

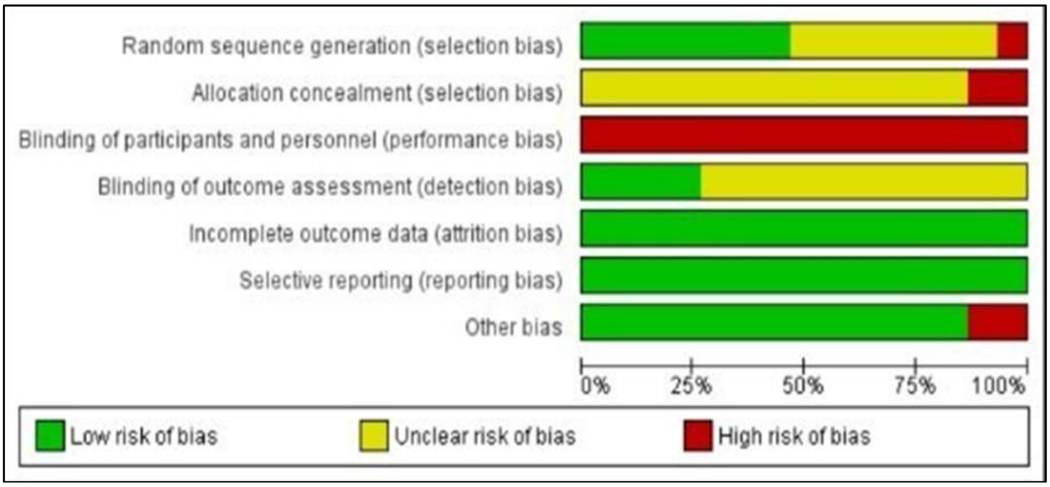



**Fig 3:** Risk of bias of included studies (N=14)

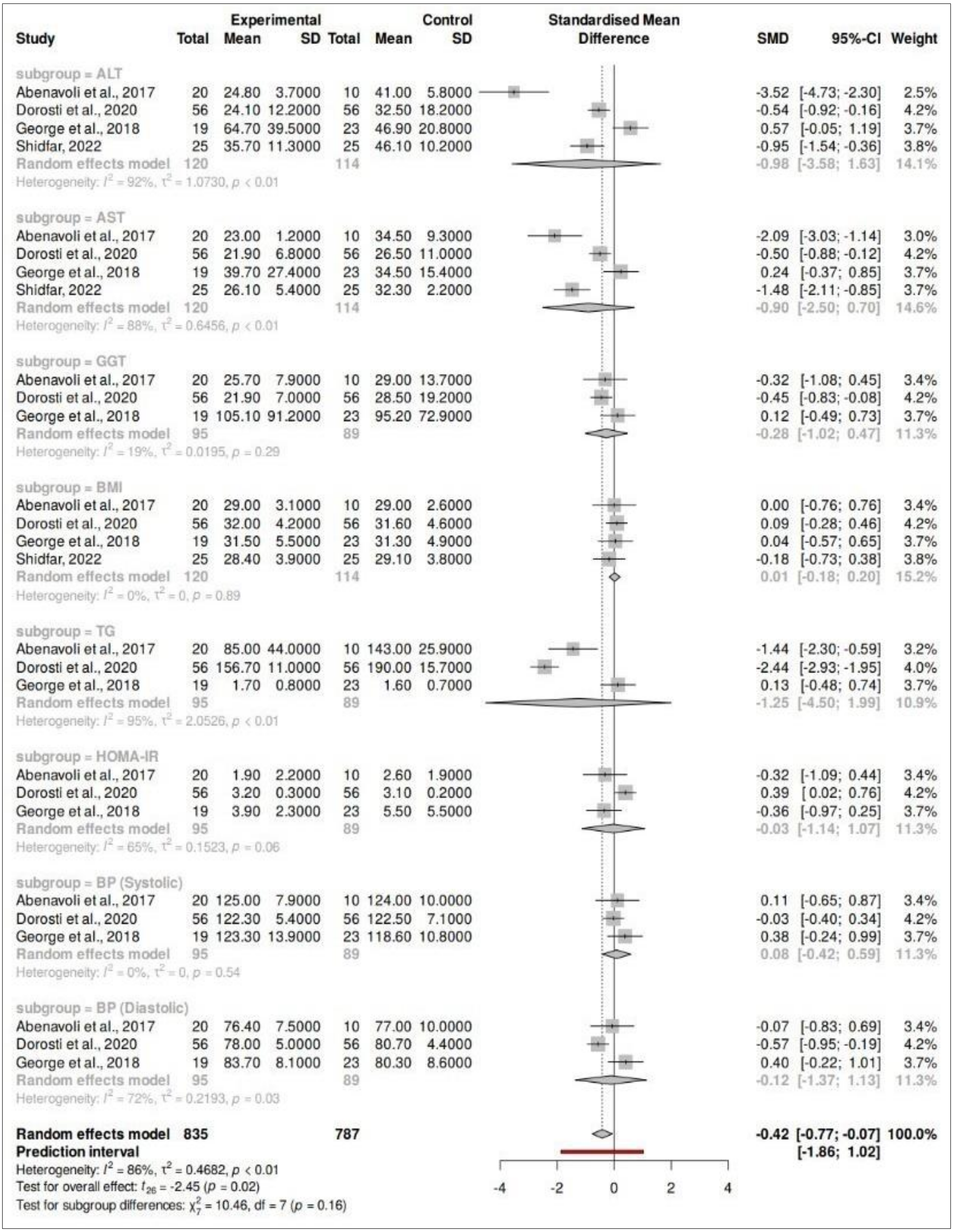



**Fig 4:** Forest plot summarizing the effects of Mediterranean Diet interventions on clinical and metabolic parameters in patients with non-alcoholic fatty liver disease (NAFLD)

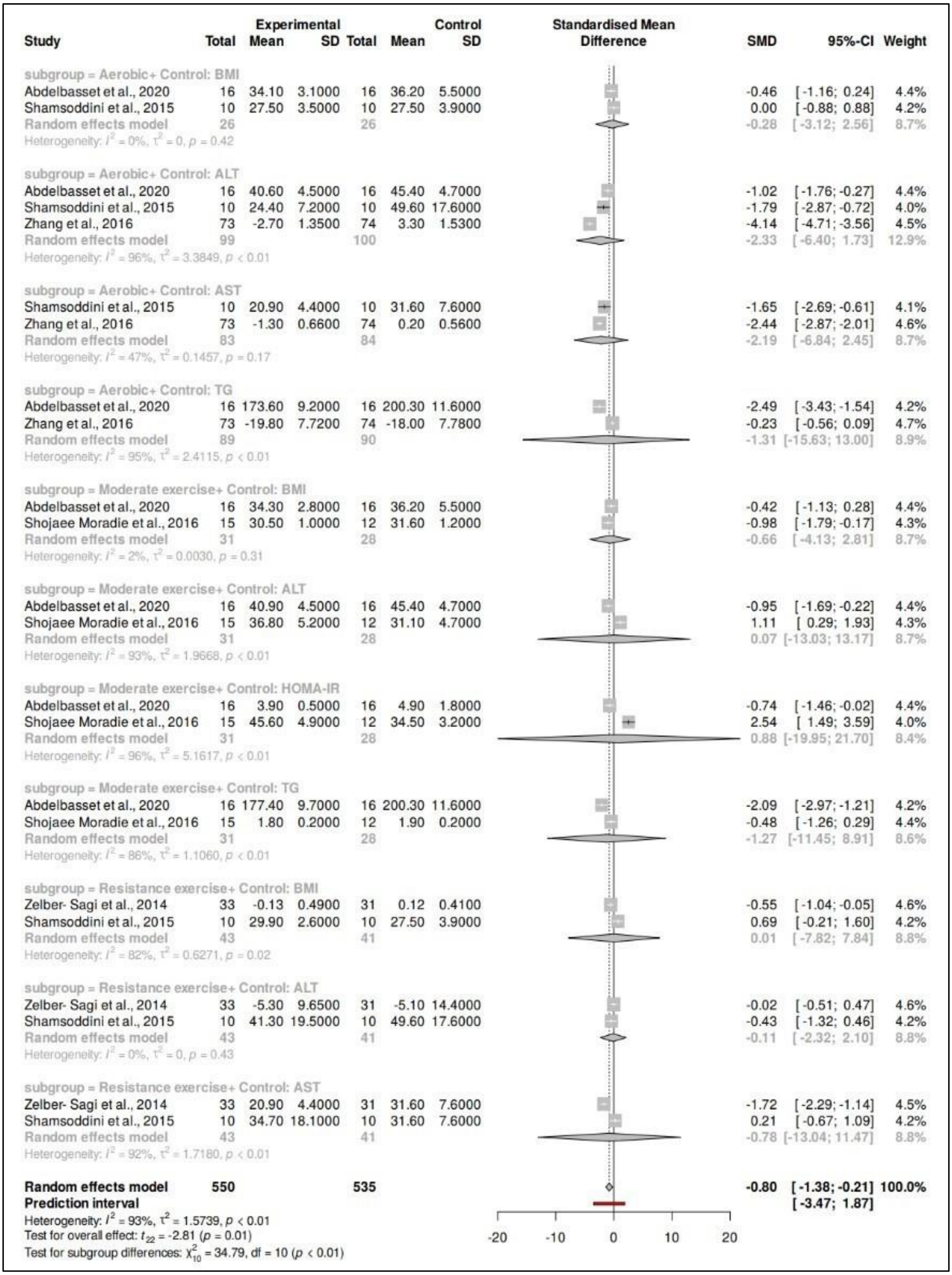



**Fig 5:** Forest plot summarizing the effects of physical activity interventions on clinical and metabolic parameters in patients with non-alcoholic fatty liver disease (NAFLD)

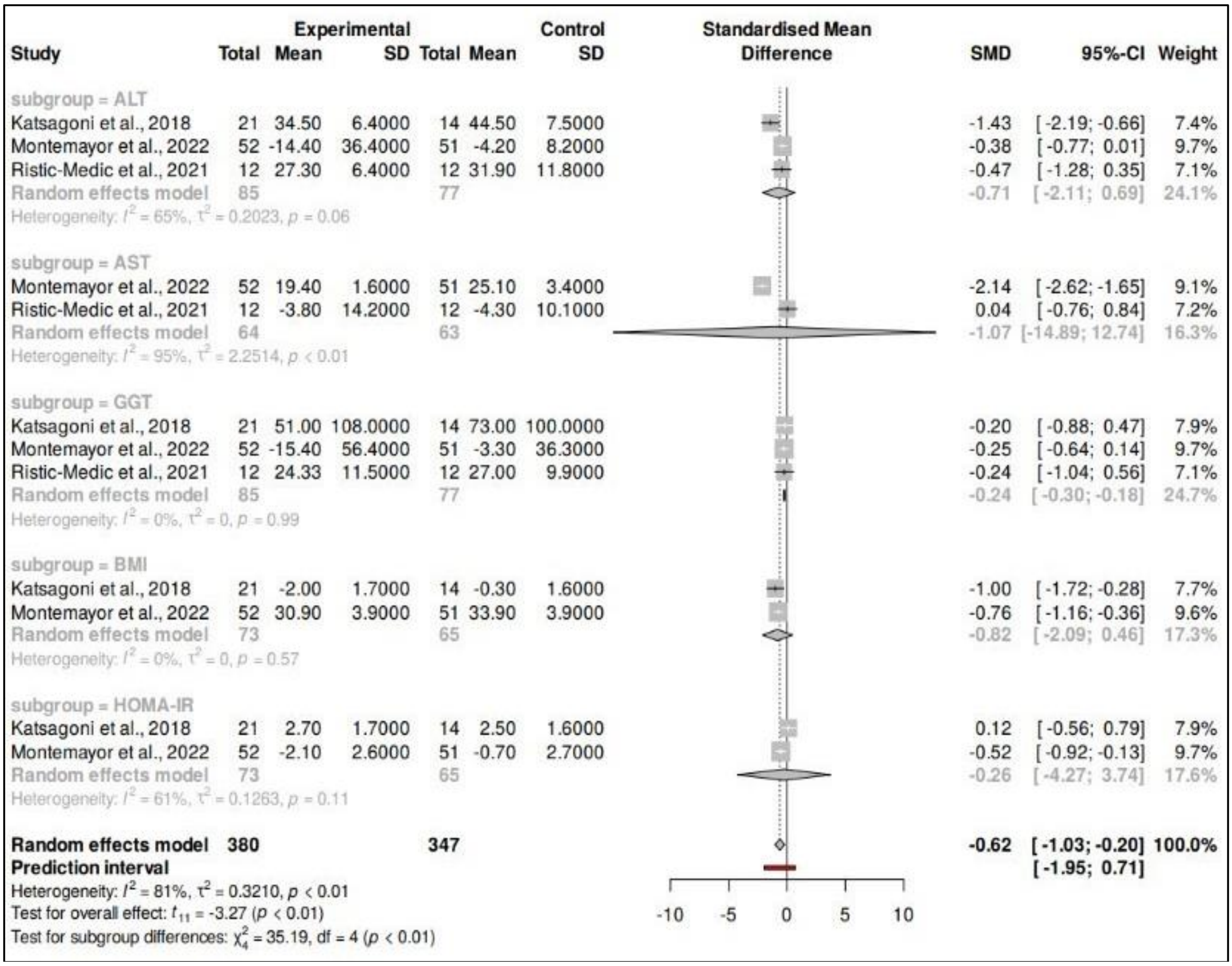



**Fig 6:** Forest plot summarizing the effects of combined interventions on clinical and metabolic parameters in patients with non-alcoholic fatty liver disease (NAFLD)

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**Conflict of Interest**
The authors declare no conflict of interest.

**Data Availability Statement**
No new data were created or analysed in this study.

**Ethics Statement**
Ethical approval was not required for this review as it did not involve human or animal subjects.

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