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FEATURE ARTICLE

LIVER HEALTH:

EVIDENCE BASED CONSIDERATIONS FOR NUTRITIONAL THERAPY AND PERSONALISED LIFESTYLE SUPPORT

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EVIDENCE-BASED CONSIDERATIONS FOR NUTRITIONAL THERAPY AND PERSONALISED LIFESTYLE SUPPORT

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ABOUT LIVER HEALTH

ABSTRACT

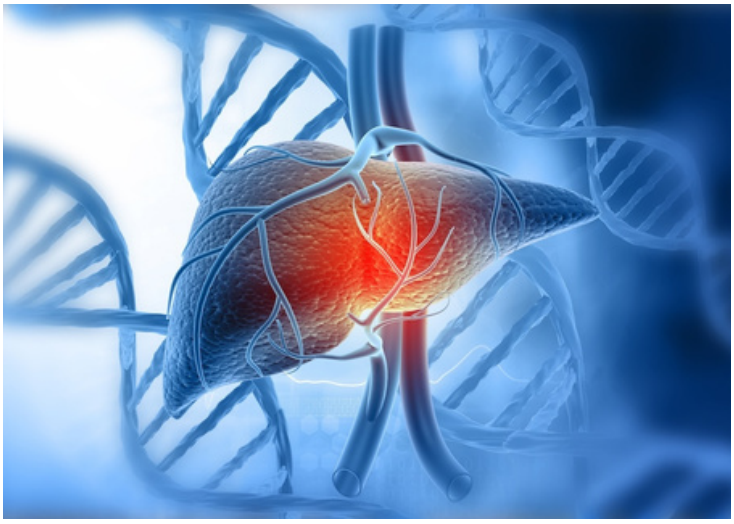
Liver health is essential for a variety of physiological processes, including transport and storage of many micronutrients. Nutritional factors, including nutrient deficiency, calorie excess and excess alcohol intake can contribute to the development of a range of liver disorders. Metabolic Associated Steatotic Liver Disease (MASLD) affects an estimated 25% of the global population and the prevalence of liver disorders is predicted to increase substantially.

This narrative review aims to provide a useful summary of common liver disorders, as well as a summary of the evidence on the role of key macro and micronutrients, dietary and lifestyle factors and the role of the microbiome in supporting liver health. It also includes a brief review of the utility of laboratory assessments for evaluating different aspects of liver health. It aims to guide evidence-based decision-making by nutrition and healthcare practitioners when recommending personalised nutrition interventions to support liver health.

INTRODUCTION

The liver is a primary metabolic organ, located in the upper right quadrant of the abdomen, responsible for critical functions including detoxification, nutrient metabolism, bile synthesis and vitamin and mineral storage. It also contributes to the regulation of immune responses, energy homeostasis, and hormonal balance. The liver's function is closely integrated with that of the gastrointestinal system, pancreas, and gallbladder.

A wide range of liver diseases and conditions can arise from diverse causes, as reviewed in the following section. For example, insufficient choline intake may cause hepatic steatosis, while other liver issues can be the result of drugs or excess alcohol intake. Metabolic Associated Steatotic Liver Disease (MAFLD) previously known as Non-alcoholic fatty liver disease (NAFLD) affects an estimated 25% of the global population and is the most prevalent chronic liver condition worldwide (1). In this review the term MAFLD will be used instead of NAFLD, even when cited research uses the latter, as NAFLD was renamed MAFLD to accurately acknowledge the role of metabolic dysfunction.



MAFLD comprises a spectrum ranging from simple hepatic steatosis to non-alcoholic steatohepatitis (NASH), fibrosis, cirrhosis, and eventually hepatocellular carcinoma (2). MAFLD is driven by metabolic syndrome and associated with obesity and diabetes (1). Pathophysiology is complex and mechanisms include hepatic lipid accumulation and insulin resistance (3) as well as oxidative stress, dysbiosis, chronic inflammation, cytokine imbalance and genetic factors (4).

Diets high in calories, refined sugar, fructose, saturated fat, trans fats, and Omega- 6 polyunsaturated fats (PUFAs) promote hepatic lipid deposition and inflammation, whereas fibre, low glycaemic-index carbohydrates, Omega 3 PUFAs, and micronutrients could have protective effects (5).

There is currently no specific pharmaceutical intervention for MAFLD. Calorie restriction, improved dietary quality, exercise, and lifestyle adjustments may all help to reduce liver fat and improve health outcomes (3).

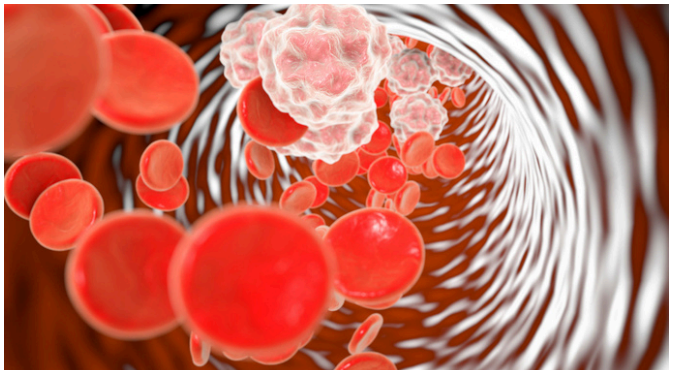
Given the modifiable nature of dietary intake, exercise and weight management, it is essential that healthcare practitioners consider nutritional status and lifestyle factors when evaluating patients with known or suspected liver dysfunction. Early identification and evidence-based dietary intervention may offer a cost-effective approach for preventing or managing liver diseases, including MAFLD.

This narrative review therefore seeks to provide a useful overview of the current evidence of the role of nutrition in liver health as well as support evidence based decision-making by nutrition and healthcare practitioners for recommending personalised nutrition interventions for liver health.

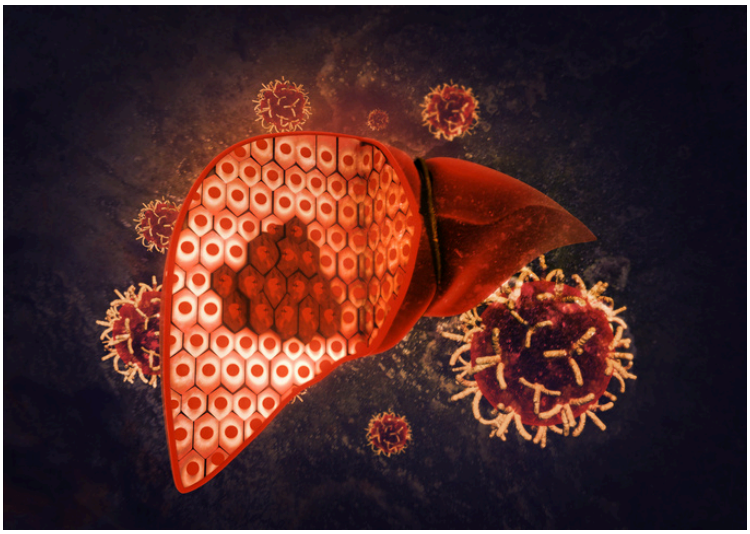
COMMON LIVER DISORDERS

WHAT ARE THE COMMON LIVER DISORDERS RELEVANT TO NUTRITION PRACTICE?

Nutritional factors, such as nutrient deficiency, excess, or toxin exposure, may contribute to a range of liver disorders including hepatic fat accumulation (steatosis). Persistent damage from these factors may provoke inflammation, hepatocellular injury, and fibrotic scarring, which can ultimately progress to cirrhosis, an irreversible stage characterised by structural alteration and loss of hepatic function (6,7).



Steatotic disorders include MASLD, alcohol-associated liver disease (ALD), and protein-deficiency–related hepatic steatosis. Non-steatotic conditions include intestinal failure–associated liver disease (IFALD), cholestatic diseases (PBC/PSC), haemochromatosis, choline-deficiency steatosis (CDS), nutritional hepatotoxicity, coeliac hepatitis and Wilson disease. Wilson disease is rare and involves impaired copper excretion, leading to hepatic copper accumulation (8).



MASLD involves hepatic steatosis, inflammation, and hepatocellular injury, and may advance to fibrosis (9). Excess energy intake, particularly from processed simple carbohydrates, promotes de novo lipogenesis (DNL), converting carbohydrates into fatty acids resulting in hepatic fat accumulation (10, 11). In a double-blind RCT (N = 94), fructose or sucrose drinks increased basal hepatic lipid secretion rates more than twofold compared with controls (median FSR %/day: sucrose 20.8 ($p = 0.0015$); fructose 19.7 ($p = 0.013$); control 9.1) (12). Increased DNL suppresses fatty acid oxidation, causing lipotoxicity, inflammation, and fibrogenesis (13). Conversely, complex carbohydrates, fibre, and wholegrains appear to be protective (14, 15).

MASLD reflects systemic metabolic dysfunction, elevating risks of fibrosis, cirrhosis, cardiovascular, renal disease, and type 2 diabetes (16). MASLD is typically asymptomatic, though upper-right abdominal discomfort and raised ALT or AST can sometimes be indicators; advanced stages can manifest with jaundice, oedema, fatigue, and abdominal distension (17, 18). Another common cause of hepatic steatosis is excessive alcohol intake in ALD, where increased NADH production inhibits fatty acid oxidation and enhances lipogenesis (19).

In choline-deficiency steatosis insufficient choline intake can cause hepatic steatosis independently of metabolic dysfunction. Choline is required for phosphatidylcholine synthesis both directly through the CDP–choline pathway and indirectly by supporting methylation via betaine. Phosphatidylcholine is essential for hepatic VLDL assembly and export; with deficiency causing intrahepatic lipid retention (20;21). Clinically, CDS resembles MASLD but occurs in lean individuals with low VLDL and plasma triglycerides, unlike the hypertriglyceridaemia and insulin resistance that are typical of MASLD (2, 22).

Severe protein malnutrition impairs apolipoprotein B and VLDL synthesis, leading to hepatic triglyceride accumulation. Subsequent refeeding, may aggravate steatosis through hyperinsulinaemia and lipogenesis, with oedema, muscle wasting, and abdominal distension (23, 24, 25). In cholestatic disease, impaired bile formation leads to hepatic and systemic retention of bile acids and bilirubin. Deficiencies in choline, taurine, or essential fatty acids may precipitate cholestasis (26). As a result, fat malabsorption leads to weight loss and fat-soluble vitamin deficiencies (27). In IFALD, prolonged parenteral nutrition induces steatosis and cholestasis through nutrient intake imbalance including excess glucose and omega-6 fatty acids, resulting in impaired VLDL export and bile metabolism (28). Hepatic inflammation and raised liver enzymes may also arise from untreated coeliac disease (29). Lastly, excess hepatic iron due to haemochromatosis or excessive vitamin A retinol intake can provoke hepatic oxidative injury and fibrosis (30, 31). Clinical management should therefore prioritise elucidating the underlying pathophysiological mechanisms and nutritional determinants, enabling the development of personalised intervention strategies that specifically address these factors.

MACRONUTRIENTS

WHAT ARE THE KEY MACRONUTRIENTS FACTORS INFLUENCING LIVER HEALTH?

The health of the liver is influenced by adequate protein intake, which supports liver repair and regeneration, immune function, metabolism regulation and maintenance of cellular homeostasis. While imbalances in macronutrient intake have been shown to impair liver health, the most effective nutritional strategies for preventing or managing conditions such as MAFLD remain to be clearly established (32).

Part of the reason for the predicted rise in liver disorders (10) may be due to the rise of obesity and the increased consumption of macronutrients, specifically saturated fat and fructose, together with insufficient protein intake and a reduction in fibre and nutrient content of the diet (33). Carbohydrates, in particular fructose added to beverages as excess calories, upregulate de novo hepatic lipogenesis. According to Lee et al., (10) total fructose-containing sugars resulted in a large increase in intrahepatocellular lipid (IHCL) in trials where excess energy from sugars was added to diets compared to the same diets without the excess sugars (13 trials; SMD: 1.72; 95% CI: 1.08, 2.36, PSMD < 0.001; no heterogeneity, I2 = 0.00%, PQ = 0.943). It was not clear if this includes fructose found in fruit, fruit juice, dried fruit and desserts.

The quality of fat in the diet also impacts liver health and disease progression. In a randomised controlled trial which investigated the impact of overfeeding on 38 participants (BMI 31± 1kg/m2, liver fat 4.7± 0/9%), overeating by 1000 kcal/day, either saturated or unsaturated fat (MUFA and PUFA) or simple sugars, showed that saturated fat increased intrahepatic triglycerides by about 55% (4.9 ± 6.6 vs. 7.6 ± 8.8%, P < 0.001) compared to 15% for unsaturated fats (4.8 ± 4.9 vs. 5.5 ± 4.8%, P < 0.02) and 33% for simple sugars (4.3 ± 4.7 vs. 5.7 ± 5.4%, P < 0.02) (34).

Using data from the NutriAct clinical trial (n = 502), Pletsch-Borba et al. (35) found that among middle-aged and older adults at risk for age-related diseases, a diet high in plant-based protein (15–25% of total energy) and unsaturated fats (15–20% of energy from MUFA and 15% from PUFA) was associated with beneficial effects on (IHCL). The improvements in liver fat and visceral abdominal fat were primarily attributed to the increased intake of unsaturated fatty acids, and these effects occurred independently of major weight loss, highlighting the importance of dietary quality.

In relation to protein, The European Association for the Study of the Liver (EASL) (36) provides clinical practice guidelines for intake, recommending 1.2-1.5 g/kg/day of protein intake for patients diagnosed with liver cirrhosis. However, a small proportion of these patients have hepatic encephalopathy, which may reduce their tolerance to animal protein (meat) and therefore vegetable and dairy proteins should be recommended. Other clinical nutrition guidance, however, is currently lacking. Recommended calorie intake for non-obese patients with cirrhosis is 35–40 kcal/kg/day; however, there are currently no recommendations regarding specific fatty acid or carbohydrate intake (32). Similarly, no specific macronutrient targets have been established for MAFLD (37).

To inform the use of macronutrients in nutritional protocols, particularly for MAFLD where pharmacological treatments remain limited, further research is needed to understand how macronutrient manipulation supports liver health. Current evidence suggests that diets high in protein and unsaturated fat, low in carbohydrate, and designed to promote weight loss are most beneficial (32, 38).

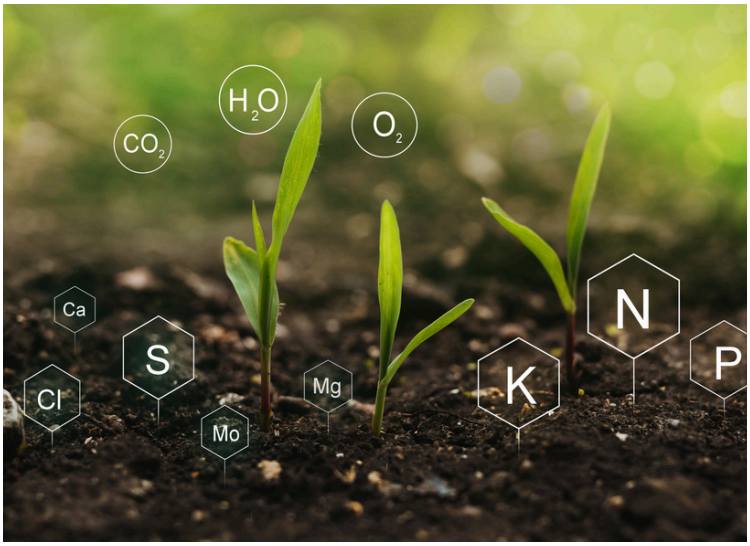
MICRONUTRIENTS

WHAT ARE THE KEY MICRONUTRIENTS FACTORS INFLUENCING LIVER HEALTH?

The liver plays a central role in micronutrient storage and homeostatic regulation, so impaired hepatic function can disrupt micronutrient metabolism and thereby contribute to disease progression (39). The liver is a key site for transport and storage of several micronutrients, including vitamin A, vitamin B12 and copper (39). Liver disease frequently leads to malnutrition due to a combination of reduced dietary intake, impaired digestion or absorption, and increased or altered metabolic demands (40). Deficiencies of fat-soluble vitamins (A, D, E and K), B-vitamins and trace elements such as zinc, magnesium and selenium are well documented in people with liver disease (41, 42), although the prevalence and pattern of deficiencies vary with the underlying diagnosis and disease severity (42).

Vitamin A is integral in liver function through its involvement in lipid metabolism, antioxidant defence, anti-inflammatory processes, and insulin sensitivity. The majority of the body's vitamin A is stored in hepatic stellate cells, underscoring the liver's role in vitamin A homeostasis (39). Liu et al. reported that reduced serum vitamin A levels were correlated with more advanced hepatic fibrosis in patients with MAFLD (43), reinforcing its protective role in liver health. Vitamin D plays multiple roles in liver health, including direct effects on liver cells, immunomodulation, antifibrotic mechanisms, and maintenance of metabolic and immune homeostasis (44). Vitamin D deficiency is consistently associated with greater disease severity. Observational studies show inverse associations between serum vitamin D and MAFLD and fibrosis (45, 46, 47). Mechanistically, vitamin D modulates hepatic inflammation and fibrogenesis (44, 48). Vitamin E, a potent lipid-soluble antioxidant, has well-documented hepatoprotective effects (49). Clinical guidelines currently only recommend vitamin E supplementation for patients with MASLD due to its ability to reduce oxidative stress and hepatic inflammation (43).

Zinc deficiency has been associated with impaired antioxidant defense, increased fibrosis risk (50, 51). Zinc contributes to hepatic protection by reducing oxidative stress, modulating inflammatory responses, and improving liver enzyme profiles in patients with chronic liver disease and MAFLD (50, 51).



Magnesium deficiency has been associated with profibrogenic activity and decreased antioxidant capacity, promoting lipid peroxidation and cytokine activation which are key pathways involved in steatohepatitis and fibrosis (52, 53). Selenium exhibits a dose-dependent relationship with liver health (43). Lower blood selenium levels were associated with an increased incidence of advanced fibrosis, whereas higher levels (>130 µg/L) were positively correlated with MAFLD and ghrelin levels, indicating a narrow optimal range for hepatoprotective benefit (43). Combined micronutrient support may therefore enhance liver health through several mechanisms.

A UK Biobank cohort analysis in individuals (n=402,476) with MAFLD, which utilised inverse probability of treatment weighting (IPTW) to account for potential confounding factors, found that habitual multivitamin use was associated with a significant lower all-cause mortality risk before (HR: 0.88, 95% CI 0.81–0.95, P = 0.034) and after (HR: 0.94, 95% CI 0.88–1.00, P = 0.037) IPTW adjustment (54). However, a meta-analysis which pooled 202 randomised trials of nutritional supplements in MAFLD found no convincing effects and concluded the evidence indicates considerable uncertainty about the effect of supplementation on clinical outcomes (55). A nuanced, personalised assessment of micronutrient status, alongside an understanding of the disease-specific mechanisms driving deficiency, is essential to clarify their contribution to liver pathophysiology and to design safe, targeted nutritional interventions to prevent or attenuate liver disease.

WHAT ARE THE KEY DIETARY FACTORS INFLUENCING LIVER HEALTH?

Excess caloric intake and insulin resistance can drive hepatic fat accumulation affecting liver health. Fat accumulation and inflammation can drive hepatic insulin resistance increasing the risk for the development of metabolic dysfunction, which is associated with MASLD (56,57).

As highlighted, increased consumption of dietary sugars, with fructose and sucrose, promotes hepatic de novo lipogenesis. In one RCT of 94 healthy men, sugar sweetened beverage consumption with moderate amounts of sucrose or fructose (80g/day) in addition to usual diet for 7 weeks resulted in a two-fold increase in hepatic fatty acid production compared to the control (median FSR %/day sucrose: 20.8; (P=0.0015), fructose: 19.7; (P=0.013), control: 9.1) (12). Glucose sweetened beverages did not have the same effect on hepatic VLDL production (median FSR %/day 11.0; (n.s)). Furthermore, low-sugar diets have been shown in one RCT of 40 adolescent boys with MASLD to result in hepatic steatosis improvements when compared to normal diet (-6.23%; 95% CI, -9.45% to -3.02%; P < .001) (58).

Fibre may act on satiety, reducing energy and fat intake (59). Fibre intake has also been shown to modulate the gut microbiota, altering bile acid production, restoring the gut barrier and inhibiting lipid absorption (60). One RCT has shown that the adoption of a high fibre (amount not given), low carbohydrate (20-25%) diet alongside dietary education amongst 44 individuals with MASLD for 2 months improved abdominal circumference, visceral fat, and body fat (P=<0.05 for all) when compared to education alone (61). Fatty infiltration of the liver was also improved (P=0.015). However, muscle mass was shown to be decreased, which could have other health implications (P=<0.05).

Liver function decline as a result of excess lipid accumulation may be mediated by mitochondrial dysfunction and the reduced capacity of the liver to transport excess lipids into circulation and increased lipid peroxidation (62).

Targeting mitochondrial function may be of benefit and diets high in polyphenols and antioxidants have been shown to benefit liver health. One RCT of 50 individuals with overweight reported that adoption of the Mediterranean diet (MD) for six months resulted in improved anthropometrics (weight, body mass index, waist and hip circumference P=0.0001 for all), lipids (cholesterol: P=0.0001, low density lipoprotein-cholesterol: P=0.005 and triglycerides: P=0.0001), hepatic fat accumulation (P=0.002), and liver stiffness (P=0.0001) compared to control (63). However, when an antioxidant supplement was introduced (silymarin 120 mg, chlorogenic acid 7.5 mg, protopine 0.04 mg, L-methionine 150 mg, and L-glutathione 10 mg), further improvements were seen on insulin sensitivity (HOMA-IR: P=0.0001) and a consistent reduction in anthropometrics was observed (waist circumference P=0.030), which may further benefit liver health. In an 18-month RCT of 294 individuals with abdominal obesity/dyslipidaemia a MD has been shown to result in intrahepatic fat loss compared to standard healthy diet (-12.2%; P=<0.001), which was doubled when enriched with polyphenols (mankai, green tea, and walnuts) and reduced red and processed meat intake (green-MD:-38.9% vs MD: -19.6%; P=0.035) (64).

A low sugar diet that is high in fibre, polyphenols, and antioxidants appears to be of benefit to liver health. However, it is also important to maintain muscle mass through exercise, which may decline with weight loss (65).

DIETARY RECOMMENDATIONS

WHAT ARE THE CURRENT DIETARY RECOMMENDATIONS FOR LIVER HEALTH?

In the UK, there are no official liver-specific dietary guidelines. The British Liver Trust and the NHS recommend a healthy, well-balanced diet for those with and for those wanting to prevent liver disease (66, 67). Their recommendations focus on maintaining a healthy body weight, optimising blood lipids, improving insulin sensitivity, and reducing inflammation which may be involved in the pathogenesis of liver disease.

As previously discussed, evidence from Abenavoli et al (68) and Meir et al (64), suggest that the adoption of a Mediterranean Diet (MD) may benefit liver health. This diet is high in monounsaturated fats, omega-3 fatty acids, fibre, and antioxidants, and may be of benefit regardless of the macronutrient content, making it an easy-to-follow pattern of eating. In one intervention study of 63 individuals with MASLD, a typical MD, low-carbohydrate MD, and low-fat MD all showed that liver enzymes and fatty liver index were improved from baseline (P=<0.05 for all), with no differences between the diets (69). Red meat and processed foods are also limited with the MD, which aligns with the NHS UK healthy eating guidelines (70).

Concerns have been raised over the suitability of diets high in saturated fat for individuals with poor liver health (71). The high saturated fat content of a ketogenic diet (KD) may seem counterintuitive, however, in the short-term, the KD has been shown to have a similar effect on liver fat content as the low-fat diet and may particularly benefit those with already established MASLD. In one RCT of 28 individuals with overweight or obesity it has been shown that the adoption of a KD for 6 weeks resulted in liver fat reductions from baseline (P=0.004) similar to individuals on a low-fat diet (P=>0.05) (72). Individuals with MASLD were shown to have more than 5% reduction in liver fat content. For individuals who are concerned, a well-planned KD, avoiding high dietary intakes of fat is possible and may still benefit liver health. In one RCT of 39 individuals with obesity, a KD high in protein (0.8-1.2g/kg ideal body weight) and low in fat (10g/day) has been shown to result in greater visceral adipose tissue loss (−21.47%± 19.1% vs. −6.33%± 28.9%; p = 0.06) and liver fat reduction (mean ± SD = −4.77 ± 4.26 vs. −0.79 ± 1.76 p = 0.0006; mean relative change = −38.5 vs. −2.7%; P= < 0.0001) compared to a standard low calorie diet (73). It is important to understand that KD success may be more apparent in men and may be affected by menopausal status in females, with benefits more apparent postmenopausally (74).

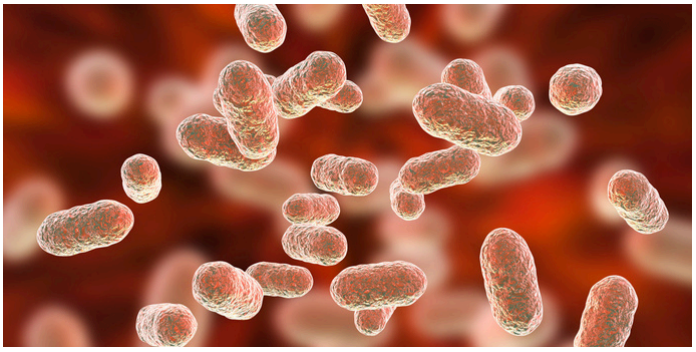
UK NHS dietary recommendations for health (70) include an emphasis on a range of fruits and vegetables. A low-fat vegan diet has been shown in one 16-week RCT of 244 individuals to result in 34.4% decreased hepatocellular lipids mean (SD) of 3.2% (2.9%) to 2.4% (2.2%) (P = .002) and 10.4% decreased myocellular lipids mean (SD) of 1.6 (1.1) to1.5 (1.0)

t(P = .03) from baseline, whilst no changes were observed in the control group with no diet changes (75). UK NHS recommendations (67) emphasise a balanced diet to support liver health, with evidence showing that MD, ketogenic, and plant-based diets may reduce liver fat and improve metabolic markers.

THE GUT MICROBIOME

WHAT IS THE ROLE OF THE MICROBIOME IN LIVER HEALTH?

The human microbiome is an ever-changing ecosystem, with significant interindividual as well as intraindividual variation (76, 77). The gut-liver axis represents a bidirectional pathway between the gut microbiota and the liver (78, 79). The liver, via the gut-liver axis, is exposed to microbial products, bile acids and nutrients making the microbiome a powerful regulator of liver health and disease (79). Three key mechanisms explain this relationship. First, the intestinal barrier acts as a first line of defence. When barrier integrity is lost, microbial components such as lipopolysaccharides (LPS) can enter circulation and travel directly to the liver, triggering immune responses which lead to inflammation. Chronic inflammation may then result in fibrogenesis (78, 80, 81). Second, microbial metabolites such as short-chain fatty acids, support the integrity of the gut lining and reduce systemic inflammation, a key factor for liver repair (82). Ammonia, ethanol and secondary bile acids elevate oxidative stress levels, damage hepatocytes and promote the progression of MASLD (78, 79). Third, immune modulation occurs when gut-derived microbial products activate hepatic pattern recognition receptors (PRR) which initiate the production of pro-inflammatory cytokines. Persistent stimulation of pro-inflammatory pathways contributes to tissue damage increasing the risk of fibrosis (79, 80).



Disruption of intestinal homeostasis and alterations in the microbiome, through these interconnected mechanisms, collectively drive the pathogenesis of liver disease, from initial fibrotic changes to end-stage cirrhosis (80, 83). Compromise of the intestinal barrier integrity and translocation of endotoxins are linked to the development of cirrhosis and hepatic encephalopathy (HE) (80, 84), where systemic inflammation and elevated ammonia levels may worsen clinical outcomes (83, 84). Disruptions in the gut microbiota can lead to overproduction of microbial metabolites including ethanol and secondary bile acids. These imbalances are key drivers in alcoholic liver disease and progression of MASLD (78, 80, 84). In parallel, sustained activation of the immune system particularly via hepatic PRR signalling results in persistent inflammation and ongoing fibrosis (80). These features are characteristics of MASLD/metabolic steatohepatitis and cholestatic liver diseases (83).

Taken together, dysbiosis emerges as a unifying factor across hepatic disorders highlighting the therapeutic potential of microbiome-targeted nutrition strategies. For instance, Ahn et al. (85) conducted a 12 week RCT in 68 obese MAFLD patients and found that a multispecies probiotic mixture significantly reduced intrahepatic fat fraction from 16.3 ± 15.0% to 14.1 ± 7.7% (p = 0.032) versus baseline. Similarly, in a meta-analysis of 15 RCTs (n = 772), probiotic-based intervention reduced serum alanine aminotransferase by a mean difference of −11.76 U/L (95 % CI −16.06 to −7.46) (86). Furthermore, in a phase II double-blind RCT of 60 patients with cirrhosis and recurrent HE, faecal microbiota transplantation significantly reduced HE recurrence (40% vs 9% in placebo, OR 0.15, 95% CI 0.04-0.64; p = 0.035) and improved gut microbial engraftment (76). These interventions can improve hepatic outcomes by correcting microbial imbalances, reducing systemic inflammation, and improving metabolic parameters. Despite promising results, variability in microbiome responses and limited long-term safety data necessitate further clinical validation (68,76;86).

The gut microbiome exerts significant influence over liver function, shaping metabolic, immune, and barrier activities along the gut–liver axis. Recognising these interactions can inform personalised nutrition interventions for the prevention and management of liver dysfunction.

HOW DO LIFESTYLE FACTORS INFLUENCE LIVER HEALTH?

Unfavourable lifestyle factors including excessive alcohol intake, smoking, physical inactivity, and adiposity are central determinants of liver health (87, 88, 89, 90, 91).

Excessive alcohol consumption strains hepatic function due to the metabolites and toxic by-products generated during alcohol metabolism (92). Alcohol-related liver disease is one of the most common and serious complications of chronic alcohol intake, with progression determined by both quantity and duration of consumption. In a Finnish cohort (n=12,368), Nivukoski et al. (89) showed that individuals who both smoked and consumed alcohol at hazardous levels had substantially higher fatty liver index scores than non-smokers who consumed alcohol, indicating additive harm to hepatic fat accumulation. Cigarette smoke promotes oxidative stress, tissue hypoxia, and systemic inflammation, all of which can accelerate hepatocyte injury and fibrosis (93, 94). A cross-sectional cohort study (n=225) by Ou et al. (95) found that smokers (n=98) had significantly higher liver stiffness on Fibroscan (10.12 ± 10.38 kPa vs. 7.26 ± 6.42 kPa, P=0.013) and smoking was independently associated with fibrosis (OR = 1.29, p = 0.015). Similarly, Jang et al. (96) observed that current male smokers had higher odds of MASLD compared with nonsmokers (OR = 1.38, 95% CI: 1.08–1.76). Moreover, participants with 10–20 pack-years had OR = 1.39 (95% CI: 1.04–1.86), and those with >20 pack-years had OR = 1.51 (95% CI: 1.14–2.00), indicating a dose-dependent relationship between cigarette exposure and MAFLD risk.

Regular exercise mitigates metabolic disturbances driving hepatic fat accumulation and fibrosis. In a 12 week randomised trial (n=18), Charatcharoenwitthaya et al. (97), demonstrated that both moderate-intensity aerobic and resistance training reduced hepatic fat content by 10.3–12.6% (95% CI) and improved insulin sensitivity independent of weight loss. Similarly, Houghton et al. (98) reported that supervised aerobic and resistance training over 12 weeks (n=24) led to a 16% relative reduction in hepatic triglyceride content and improvements in ALT compared with standard care. Exercise also lowers systemic inflammation and oxidative stress, both key contributors to fibrosis progression (98). In contrast, sedentary behaviour independently increases the risk of MASLD (100). In their randomised crossover trial, Duvivier et al. (101) found that replacing sitting with brief bouts of light walking, for just 3 minutes every 30 minutes, significantly improved postprandial glucose and triglyceride responses in a crossover study of 19 participants with type 2 diabetes.

Emerging research highlights the role of sleep quality, stress regulation and circadian rhythm alignment in maintaining liver health. Poor or insufficient sleep adversely affects insulin sensitivity and inflammatory activity, independently increasing the risk of developing MASLD (102). Disrupted circadian rhythms, common among long-term shift workers or individuals with irregular or late-night eating patterns, can alter hepatic gene expression governing glucose and lipid metabolism, promoting steatosis, oxidative stress, and inflammation (103,104). Additionally, chronic psychological stress activates the hypothalamic–pituitary–adrenal axis, leading to elevated glucocorticoid levels that impair glucose and lipid metabolism, promote hepatic fat accumulation, and exacerbate oxidative stress and inflammation (105, 106). Consistent with this, large-scale cross-sectional research in 171,321 adults reported that higher perceived stress levels were significantly associated with increased prevalence of MASLD (OR = 1.17, 95% CI), independent of body mass index and lifestyle factors (107).

Adopting a health-promoting lifestyle remains the cornerstone of liver health. Evidence consistently shows that regular physical activity, adequate sleep, and avoidance of alcohol and tobacco significantly

reduce the incidence and progression of liver disease. Promoting these behaviours may protect hepatic function, improve quality of life, and reduce the long-term risk of fibrosis, cirrhosis, and related metabolic complications.

LIVER TESTING

WHAT TESTS ARE AVAILABLE TO ASSESS LIVER FUNCTION?

Liver function tests (LFTs) are used to evaluate different aspects of liver health, including hepatocellular injury, cholestasis, and the liver's ability to synthesise and excrete essential substances. To assess these functions, several biochemical markers are measured. The enzymes alanine aminotransferase (ALT) and aspartate aminotransferase (AST) primarily reflect hepatocellular injury, as they are released into the bloodstream when liver cells are impaired. Alkaline phosphatase (ALP) and gamma-glutamyl transferase (GGT) are markers of cholestasis and indicate obstruction or impairment of bile flow. Total and direct bilirubin levels evaluate the liver's excretory function, while albumin and total protein concentrations provide information about its capacity to synthesise essential proteins such as albumin and clotting factors (108).

Reference intervals for LFTs vary based on population, methodology (109) and the intended purpose, such as diagnosis or health optimisation; while variables including age, sex and ethnicity influence the partitioning and the interpretation of those intervals (110, 111, 112). Each laboratory sets and verifies its own reference intervals based on their methods, instruments, population, and calibration. Thus, there can be differences among laboratories in upper or lower limits for the same analyte (113), including public and private NHS laboratories and this is standard practice in laboratory medicine (114).

NHS laboratories reference intervals appear to be attributed to the Pathology Harmony initiative (115, 116) aiming to reduce variation and adopt common, evidence-based reference intervals across labs drawing on multicentre datasets, such as NORIP and IFCC-traceable methods. Private UK providers generally align with the same principles and intervals (115, 117) as they must be accredited by UKAS, which requires the use of validated and traceable reference intervals consistent with national or international standards (such as those developed under IFCC or NORIP).

An improved strategy for identifying abnormal liver test results (iLFT) using a laboratory algorithm was first introduced in NHS Tayside, Scotland (118). This same approach was later applied in a population-based study (119), that found that 33% of individuals with MASLD and advanced fibrosis had ALT between 31 and 54 U/L, who would not have been all identified using the NHS standard ALT range of <40 U/L (120). This reflects later evidence indicating that higher ALT values are associated with an increased risk of hepatic steatosis and metabolic syndrome, thereby setting the upper healthy limit at <22 U/L for women and <34 U/L for men (121, 122).

The reference intervals used by the NHS, along with the ranges commonly applied by private laboratories for each biomarker in the standard LFT panels, are shown in Table 1.

It is worth noting that, nutrition and lifestyle medicine practitioners use laboratory testing for the purpose of health optimisation (123, 124) while NHS assessments mainly focus on excluding disease (113). In the context of health optimisation, the focus is placed on identifying subclinical dysfunction, often using additional markers that are not liver function measures per se. Additional markers are used to infer broader metabolic or "functional" liver health and these may include high sensitivity CRP, ferritin, oxidative stress markers, homocysteine, glutathione and others.

Assessing liver function through LFTs, alongside metabolic markers, provides valuable contextual

TABLE 1

Reference intervals for adults, used by the NHS and public labs (120) and ranges of intervals used by private laboratories (122).

Marker	*NHS/ public laboratories*	*Private laboratories/ literature*
ALT	0 – 40 U/L	19 U/L (women) and 30 U/L (men)
AST	0–32 U/L (women), 0–40 U/L (men)	13–37 U/L (women) and ~14–45 U/L (men)
ALP	30 – 130 U/L	ALP 37–106 U/L
GGT	0–50 U/L(women), 0–90 U/L (men)	<77 U/L (women <40); <64 U/L (women ≥40); <78 U/L (men <40) and <114 U/L (men ≥40)
Total and Direct (Conjugated) Bilirubin	Total 2 – 21 umol/L; Direct <4 umol/L	5–24 µmol/L
Albumin	35 – 50 g/L	37–48 g/L (<40 y), 37–46 g/L (40–70 y), and 35–46 g/L (>70 y)
Total Protein	60 – 80 g/L	62–78 g/L

information in nutrition practice. Liver function markers may reveal patterns to help identify hepatic inflammation, metabolic dysfunction, steatotic tendencies or impaired bile flow. These insights can support more precise nutritional recommendations and indicate when medical referral is appropriate. By evaluating LFTs alongside clinical history and diet-lifestyle assessment, practitioners can identify suitable interventions, such as modulating dietary carbohydrate and fat quality, adjusting protein intake or supporting weight management, to support metabolic health and enhance liver function and detoxification capacity.

SUMMARY

THE ROLE OF NUTRITION PRACTITIONERS IN SUPPORTING LIVER HEALTH

Nutritional practitioners are well positioned to support individuals' health through personalised nutrition and lifestyle interventions, particularly when these interventions target the specific pathophysiological mechanisms most relevant to the individual. Nutritional excesses, deficiencies, and toxin exposures can contribute to multiple liver disorders by inducing hepatic steatosis, inflammation, and fibrosis. Nutrition practitioners can therefore play a key role in supporting individuals with liver conditions by

applying evidence-based dietary and lifestyle strategies that modulate the mechanisms underpinning these disorders.

Pathophysiological mechanisms differ across non-steatotic liver diseases, reflecting heterogeneous aetiologies, whereas steatotic disorders such as MASLD are primarily driven by metabolic dysfunction, insulin resistance, inflammation, increased de novo lipogenesis, oxidative stress, mitochondrial dysfunction, and progressive hepatocellular injury. Macronutrient intake directly influences these mechanisms; for example, excessive consumption of simple sugars (particularly fructose) promotes steatosis, and high saturated fat intake can elevate intrahepatic triglyceride levels. In contrast, adequate intake of protein, fibre, omega-3 polyunsaturated fatty acids, and antioxidant-rich foods appears protective. Vitamins D, A, and E, as well as zinc, selenium, and magnesium, also contribute to liver health. A personalised assessment of micronutrient status is therefore essential for understanding its impact on liver function and guiding targeted nutritional interventions.

Although the UK does not have liver-specific dietary guidelines, NHS recommendations emphasise a balanced diet to support liver health (67). Beyond macronutrient quality, nutrition practitioners should consider evidence for dietary patterns such as the Mediterranean diet, ketogenic diet, and plant-based diets, which can reduce hepatic fat and improve metabolic markers. Total caloric intake should also be addressed, particularly when obesity is a comorbidity. The gut microbiome strongly influences liver health through regulation of intestinal barrier integrity, production of shortchain fatty acids, and modulation of the immune system. Dysbiosis is increasingly recognised as a shared mechanism across liver diseases, highlighting the therapeutic potential of nutritional strategies that restore gut–liver axis homeostasis and reduce hepatic injury.

Lifestyle factors, including regular physical activity, adequate sleep, and avoiding alcohol and tobacco, are consistently shown to reduce liver disease risk and slow disease progression. Engagement with these behaviours can help mitigate fibrosis, cirrhosis, and other damaging pathophysiological processes. By integrating tailored nutritional and lifestyle interventions, practitioners can provide comprehensive support for individuals with liver conditions. A range of liver function tests can offer insight into hepatic inflammation, steatosis, metabolic dysfunction, and bile flow, enabling nutritional practitioners to refine personalised interventions and determine when medical referral is warranted.

KEY PRACTICE POINTS FOR NUTRITIONAL THERAPISTS

- **Personalised support:** Target dietary interventions, with a food first approach which aims to ameliorate key mechanisms of pathophysiology, while considering individual needs and preferences.
- **Address macro and micronutrient intake:** ensure balance of macro and micronutrients nutrients with specific focus on sufficient dietary intake of protein, fibre, Omega 3 PUFA, antioxidants and vitamin D.
- **Address gut health:** as well as liver health consider the gut and promote a healthy gut microbiome, enhance gut barrier function and support immune function.
- **Address lifestyle factors:** promote exercise, weight loss, sleep hygiene and the removal of alcohol and tobacco.
- **Work collaboratively:** Collaborate closely with the multidisciplinary team to integrate nutrition care with medical management, monitor for complications such as hepatic encephalopathy, and adjust nutrition plans accordingly.

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MB conceived of the review, wrote the abstract, introduction and summary, contributed to all sections of the article, provided comments to authors and revised the content. AP, CS and SC each researched and wrote two sections of the article. NE & APA each researched and wrote one section of the article. KL contributed to planning, design and revising the final content. All authors reviewed and accepted the final manuscript.

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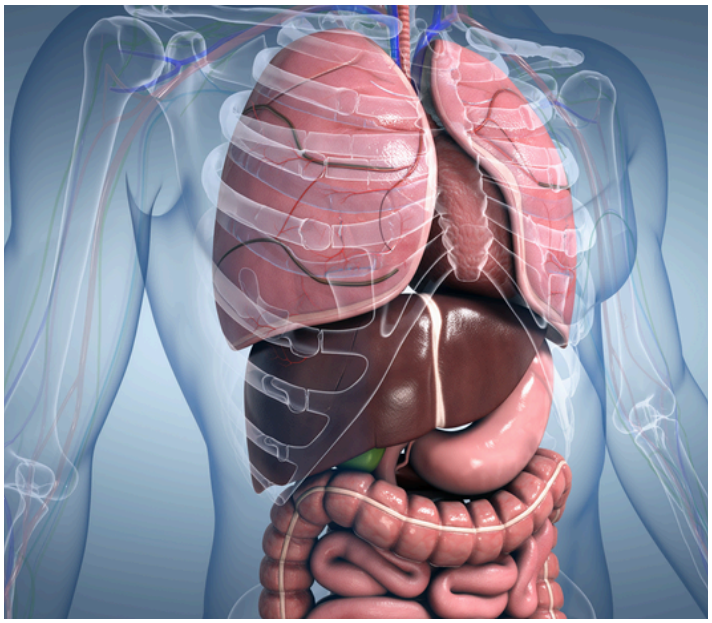

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