

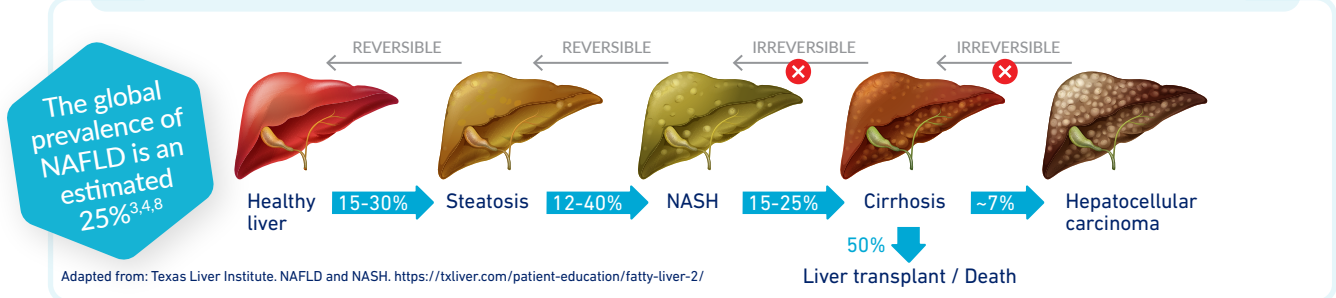
WEIGHT LOSS AND IMPROVED LIVER HEALTH

What is NAFLD?

Non-Alcoholic Fatty Liver Disease (NAFLD) is an umbrella term which encompasses a spectrum of conditions, ranging from steatosis to cirrhosis and is characterized by the presence of excessive hepatic fat accumulation $\geq 5\%$ and associated with insulin resistance in the absence of other recognized causes of fatty liver (e.g., alcohol, virus, drugs, autoimmunity).^{1,2,8,11}

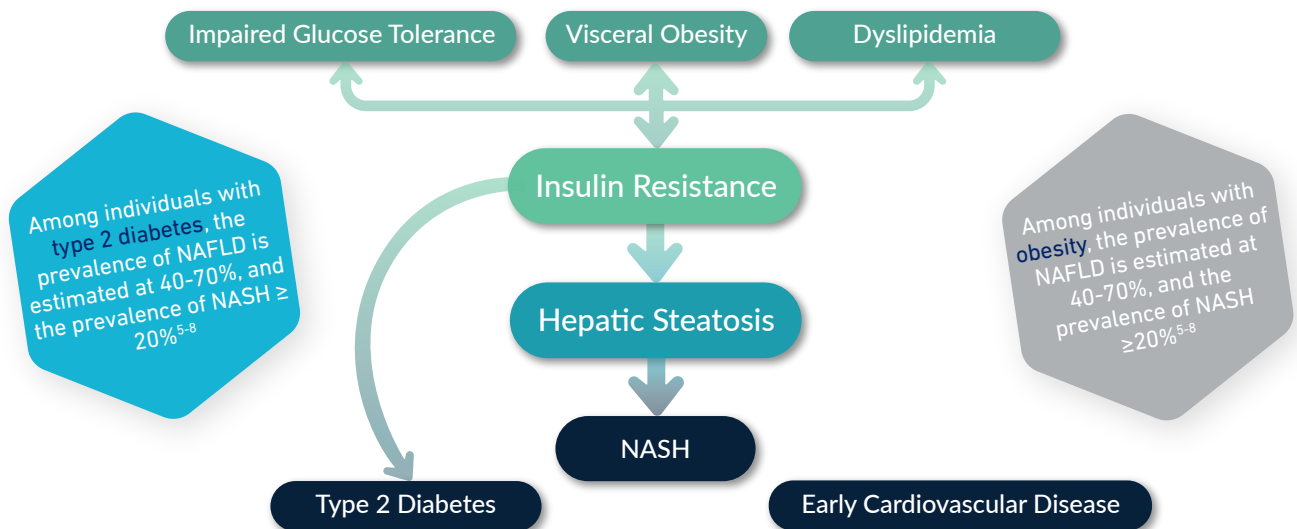
Non-Alcoholic Steatohepatitis (NASH) is an advanced form of fatty liver disease defined by the presence of hepatic steatosis with hepatocyte damage and inflammation that can progress to fibrosis, cirrhosis, and hepatocellular carcinoma which may require a liver transplant.^{1-5,7,12} By 2030, NASH-related cirrhosis will be the leading cause for liver transplants in the US.⁴

SPECTRUM OF LIVER DISEASE ASSOCIATED WITH METABOLIC CONDITIONS

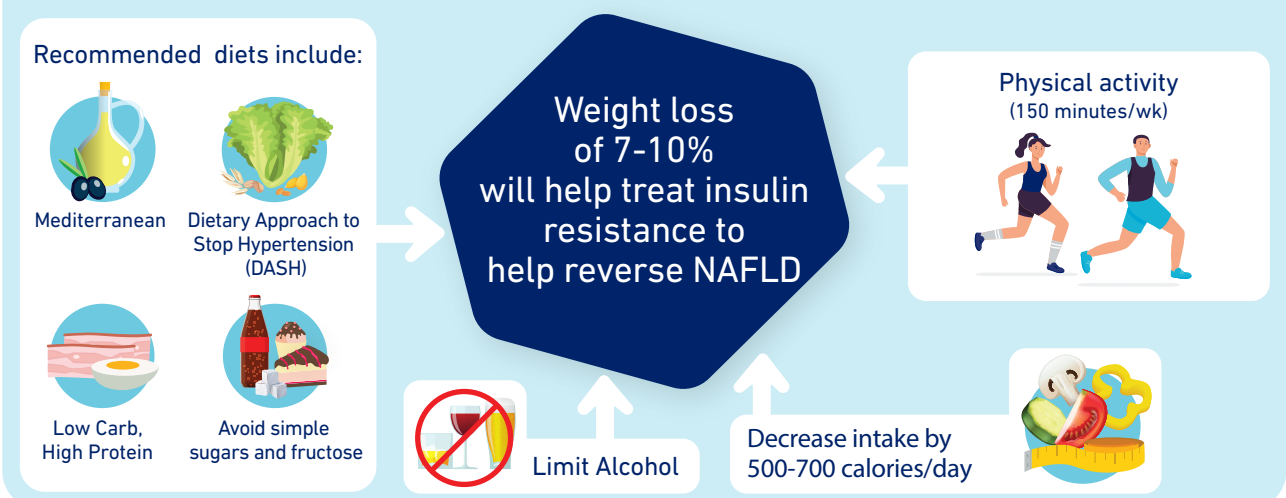


Insulin resistance is central to the development of NAFLD

NAFLD is associated with cardiovascular disease and type 2 diabetes^{3,7}



The Clinical Practice Guidelines of expert panels recommend lifestyle intervention of energy restriction, diet modification, and physical activity to reduce weight^{2,10}



Feasibility of a Very Low-Calorie Diet to Achieve a Sustainable 10% Weight Loss in Patients With Non-alcoholic Fatty Liver Disease

Scragg J., et al. *Clinical and Translational Gastroenterology* 2020;11: e00231. <https://doi.org/10.14309/ctg.000000000000231>

Introduction

Nonalcoholic fatty liver disease (NAFLD) is the most common liver condition worldwide, affecting an estimated 25% of people worldwide. There are no approved pharmacological interventions available for NAFLD. Lifestyle and diet modification with a weight loss goal of +10% are the primary recommendations for treating NAFLD; however, only a minority of patients achieve this level of weight reduction with standard dietary approaches.

The primary aim of this study was to determine whether a low-calorie diet (VLCD) is an acceptable and feasible therapy to achieve a >10% weight loss and sustained for at least 6 months in patients with clinically significant NAFLD.

Methods

- Patients (n=45) were recruited from hepatology clinics within the Newcastle upon Tyne Hospitals NHS Foundation Trust between January to July 2019
- Inclusion Criteria
 - Adults ≥ 18 year
 - Diagnosis of clinically significant NAFLD defined using imaging Fibroscan of steatosis plus one of the following:
 - An indeterminate or high NAFLD Fibrosis Score (NFS) ≥ 1.455
 - Fibrosis-4 score (FIB-4) ≥ 1.3 if age ≤ 65 years; ≥ 2.0 if age ≥ 65 years
 - Histological evidence of NASH with fibrosis
 - Compensated NASH cirrhosis (Child-Pugh score ≤ 7)
 - Stable weight and body mass index (BMI) ≥ 27 kg/m²
- Exclusion Criteria
 - Evidence of coexisting liver disease or decompensated NASH cirrhosis (Child Pugh score ≥ 7)
 - Treatment with antiobesity drugs or insulin to manage T2DM
- Primary Outcomes:
 - Feasibility and acceptability of a VLCD intervention, recruitment and retention
 - Percent of patients that achieve $\geq 10\%$ weight loss, sustained for ≥ 6 months post VLCD intervention.
- Secondary Outcomes:
 - Absolute change in body weight and body composition
 - Change in liver stiffness (Fibroscan)
 - Change in cardiovascular disease (CVD) risk (QRISK2/blood pressure/lipids)
 - Change in T2DM risk (HbA1c/HOMA-IR/glucose/medication changes)
 - Weight-related QoL at 9 months (Obesity and Weight Loss QoL Instrument and Weight-related Symptom Measure)

Intervention

- At the start of the VLCD, any sulfonylurea oral hypoglycemic agents were discontinued. All other diabetes medications were continued as normal.

VLCD Intervention phase

- An 8-week VLCD intervention (~ 800/kcal/day) using OPTIFAST® total meal replacement products (fat 19.4%; carbohydrate 43.4%; fiber 3.5%; protein 33.7%)
 - If unable to maintain consistent compliance due to external factors VLCD was extended an additional 4 weeks (a maximum of 12 weeks)
- Patients were encouraged to eat 3 portions (240g) of nonstarchy vegetables and to drink at least 2 L of water or calorie-free beverages each day
- Weekly one-to-one support was provided throughout the VLCD phase using a combination of phone calls, emails, and face-to-face appointments
- Dietary compliance was monitored by change in body weight

Food reintroduction phase

- Stepped food reintroduction for 4 weeks
 - For 2 weeks, 1 food-based meal replaced 1 meal replacement product; for weeks 3 and 4, 2 food-based meals were reintroduced
 - To prevent weight gain, lifestyle behavior change support and nutrition education was provided
- Increased physical activity was recommended during the food reintroduction and weight maintenance phases

Weight maintenance phase

- Monthly/bimonthly clinic visits to measure blood pressure, weight, blood glucose, lipids, and liver enzymes
- Participants remained on an individualized food-based diet to prevent weight regain and support weight stabilization and/or further weight loss

Results

- 30 out of 45 (67%) patients were enrolled in the study; 27 (90%) completed the VLCD phase; 20 (67%) completed the study to the 9-month follow-up period
- 34% (n=10) achieved and maintained $\geq 10\%$ weight loss at 9-months (ITT); Mean weight loss was 10.3 kg (23 lbs) or 9%
 - 51% achieved $\geq 7\%$ weight loss at 9 months
 - 68% achieved $\geq 5\%$ weight loss at 9 months
- Mean BMI decreased from 42 kg/m² to 35 kg/m²; % change in total body fat decreased from 45% to 41%
- Among completers of the VLCD phase, liver health (liver enzymes and liver stiffness), CVD (overall blood pressure and QRISK2), metabolic health (fasting glucose, HbA1c, and insulin), and body composition significantly improved and was maintained to 9-months
- Overall QRISK2 reduced significantly from 15.5% to 13.3%, suggesting a global improvement in 10-year CVD risk
- 17% of patients decreased their diabetes medication at 9-months; 10% (n=3) discontinued all DM medications
- Weight-related QoL score and weight-related symptoms score were significantly improved at 9-months

Conclusion

- This study confirms that a VLCD intervention, such as OPTIFAST®, along with behavioral modification and lifestyle counseling can be an option for individuals with NAFLD to enable significant and sustainable weight loss, and improve liver health and quality of life, while also decreasing cardiovascular disease risk.

Nestlé Health Science provided OPTIFAST® product for this study

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