

## Non-alcoholic fatty liver disease is on the rise in tandem with growing levels of obesity and diabetes

NAFLD (or Non-Alcoholic Fatty Liver Disease) is the accumulation of excess fat in the liver and is now the commonest cause of liver disease in Western countries due to the rapid rise in levels of obesity and type 2 diabetes (T2DM). NAFLD is a major European health burden due to its high prevalence - NAFLD affects 1 in 4 across the EU – and capacity to progress to liver cirrhosis and liver cancer, and because it is associated with a greater risk of cardiovascular disease and other cancers.

NAFLD may develop as:

- **Simple steatosis (fat): the accumulation of fat in the liver without damage or inflammation. It may slowly progress to liver inflammation and scar tissue (fibrosis) over many decades.**
- **Non-Alcoholic SteatoHepatitis (NASH): the accumulation of fat in the liver causes inflammation, resulting in cellular damage to the liver cells, switching on fibrosis genes, resulting in liver scarring. NASH is considered to be the more progressive and aggressive subtype of NAFLD and can lead to the development of fibrosis and cirrhosis.**

The presence of fibrosis is the most important determinant of liver outcome. Over a 10-year follow up period, 21-28% of patients with NASH compared to just 4% of patients with simple steatosis developed cirrhosis and related complications such as hepatocellular carcinoma (HCC). Patients with NAFLD have an increased risk of dying from liver disease, cardiovascular disease and most causes of cancer, with modelling suggesting that the annual predicted economic burden of NAFLD in Europe would be >€35 billion of direct costs and a further €200 billion of societal costs.

More than half of adults and one third of children in Europe are classified as overweight or obese, with the proportion being highest in those from lower socio-economic groups. Unhealthy behaviour, including a lack of physical activity and excess calorie intake together with high consumption of fructose and saturated fats leads to weight gain, which plays a major role in the development and progression of NAFLD. Moreover, children and adolescents that are

overweight are at greater risk of staying overweight as adults. Sugar-sweetened beverages (SSBs) are one of the largest sources of added sugar and, whilst an important contributor of calories, have few, if any, other nutritional value. Consequently, consumption of SSBs is now one of the leading causes of childhood and adult obesity and is associated with NAFLD and increased liver damage. A recent study, modelled on a 20% levy on SSB in the UK, estimated that it would prevent 3.7 million cases of obesity and 25,498 cases of BMI-related disease over the next 10 years (2015-2025), thus avoiding £10million in National Health Service costs in 2025 alone.

Across the WHO European Region, children are regularly exposed to marketing that promotes foods and drinks high in energy, saturated fats, trans-fatty acids, added sugar (meaning refined sugars: sucrose, fructose and high fructose corn syrup - HFCS incorporated into food and beverages) or salt. Such targeting of children/adolescents to food and beverage commercials, and in particular those embedded in children's TV programmes, electronic media, including video games, DVDs and social media such as Instagram and YouTube have been demonstrated to drive consumption of high-calorie and low-nutrient beverages and foods. Of note, sugar-sweetened beverages (SSBs) are one of the largest sources of added sugar and an important contributor of calories with few, if any, other nutrients. Consequently, consumption of SSBs is now one of the leading causes of childhood and adult obesity, and is associated with NAFLD and increased liver damage (NASH and fibrosis) in NAFLD patients. Research indicates that governmental measures aimed at increasing the cost of SSBs can reduce consumption and decrease weight. In addition, saturated fat consumption increases

# FibroScan®

liver fat, in contrast to healthier fats as mono and poly-unsaturated fats, such as in the Mediterranean diet which is beneficial in the treatment of NAFLD, characterized by a high intake of olive oil, nuts, fruits & vegetables, legumes and fish and a low intake of red and processed meat, and added sugar.

Lack of physical activity and increasing sedentary behaviour are becoming a growing concern in both children and adults, resulting in excessive adiposity and type-2 diabetes. Physical activity, both aerobic and resistance training, produces significant changes in liver fat, which, along with the strong cardiovascular benefits, make it an essential adjunct to healthy eating. Just as the marketing environment influences eating behaviour, the built environment influences physical activity. Establishment of a safe and appealing walking and cycling infrastructure can have a major influence on behaviour, with the recent World Health Organisation Global Action Plan on Physical Activity (10) providing a framework to support policy and practice in this area.

## DIAGNOSIS:

Although an elevated ALT (liver blood test) can indicate hepatic inflammation in patients with NAFLD, patients with advanced fibrosis frequently have normal LFTs. Almost three quarters of T2DM patients with NAFLD and half of those with NASH have normal ALT levels. Consequently, normal LFTs in diabetic patients should not reassure the clinician that there is no evidence of liver disease. Abdominal or liver ultrasound is commonly the means by which a fatty liver is identified. Ultrasound is a widely available and inexpensive diagnostic tool for the presence of fat in the liver, but cannot identify or quantify fibrosis (liver scarring).

Vibration controlled transient elastography (tradename FibroScan®) is an ultrasound-based technology which measures liver stiffness and correlated with liver fibrosis. Several studies have compared paired liver biopsies and FibroScan® results in more than 1,000 patients and have shown that FibroScan® is reliable in distinguishing advanced fibrosis from mild or no fibrosis. In one recent study of 1,918 Chinese type 2 diabetic patients assessed by FibroScan®, 73% had liver fat scores above the upper limit of normal, and 18% had liver stiffness scores indicative of advanced fibrosis/cirrhosis. FibroScan® assessment is therefore a very attractive non-invasive method of assessing liver fibrosis. It also has the advantage of tracking changes over time and changes in response to treatment.



## TREATMENT:

Currently, there are no licensed pharmacological therapies for NAFLD. The main focus of treatment therefore is lifestyle intervention including diet, exercise (aerobic and resistance), and behavioural change. A number of studies have reported that in overweight patients with NAFLD, 7–10% weight loss sustained over 48 weeks results in significant improvement of liver blood tests, reduction in liver steatosis (fat) and inflammation, and a significant reduction in histologic severity of NASH. Therefore, lifestyle intervention can improve and reverse NASH, provided significant weight loss is achieved. However, unless patients with NAFLD are identified and diagnosed, they are denied the knowledge and opportunity to make the necessary changes.

### Healthy Eating

Consumption of saturated fat increases liver fat. In contrast, healthier mono and poly-unsaturated fats, such as in the Mediterranean diet (characterised by a high intake of olive oil, nuts, fruits, vegetables and fish and a low intake of red and processed meat and added sugar) are beneficial in the treatment of NAFLD.

### Exercise

Physical activity produces significant changes in liver fat making it an essential complement to healthy eating. Establishment of safe walking and

cycling infrastructures can have a major influence on behaviour, with the recent WHO Global Action Plan on Physical Activity providing a framework to support policy and practice in this area.

### Education

Awareness that obesity and diabetes can lead to significant liver disease is low amongst the public and the medical community, as is knowledge of appropriate and effective behaviour change techniques to avoid relapse and weight regain.

### Industry Regulation

Food and beverage manufacturers have a social responsibility to protect consumers. Research indicates that governmental measures aimed at increasing the cost of SSBs can reduce consumption by 20-50%. It is estimated that a 20% levy on SSBs would prevent 3.7 million cases of obesity and 25,498 cases of BMI related disease over the next 10 years, saving approximately €11.5m in health service costs.

### RECENT RESEARCH ON NAFLD:

Researchers from Bristol University tested more than 4,000 young people enrolled in a longitudinal study called the “Children of the 90s”, set up to follow the lives and health of children born in 1991 and 1992 in Avon, England. All of them had been given an ultrasound at the age of 18, which revealed that 2.5% had non-alcoholic fatty liver disease. Five years later, a newer kind of scan called transient elastography or FibroScan® detected that over 20% had fatty deposits on the liver, or steatosis, indicating non-alcoholic fatty liver disease. Half of those were classified as severe. The scans also found that 2.4% had fibrosis – scarring on the liver. Severe scarring can cause cirrhosis.

Presenting the results of the study at the International Liver Congress in Vienna in 2019, Dr Kushala Abeysekera, from the University of Bristol, said: “We were concerned to find that, at only 24 years of age, one in five had steatosis and one in 40 had evidence of fibrosis, based on elastography results, in a group of largely asymptomatic, predominantly Caucasian young people. The results of our study suggest greater public health awareness of non-alcoholic fatty liver disease is needed in young adults in the UK”. He told the Guardian they did not expect to see these levels of disease in young people. “Nobody has looked at them with FibroScan® before. This is a blind spot in clinical practice,” he said. “We don’t look because they are unlikely to have any complications of it”. They needed more data and would be following up the young people in the study, he said, but “this is potentially a harbinger of things to come. We may see an increase in severe advanced liver disease. It may shift from the 50s and 60s to the 40s and 50s because of the epidemic.” The vast majority of the young people with non-alcoholic fatty liver disease were overweight, with a BMI over 25. Among people with the largest amount of fatty liver deposits, 60% were obese.

### WORLD OBESITY DAY – 11<sup>th</sup> October 2019



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Ref: EASL policy statement on food, obesity and non-alcoholic fatty liver disease (NAFLD) 04-04-2019