NAFLD AND NASH

Testing options to help identify NAFLD and NASH

labcorp

NAFLD AND NASH

There is a growing, unmet need in chronic liver disease.

Non-alcoholic fatty liver disease (NAFLD) is a collective term used to describe a group of conditions where there is an abnormal accumulation of fat in the liver in those who drink little to no alcohol. This may range from a non-serious condition called fatty liver to a potentially serious condition called non-alcoholic steatohepatitis or NASH.[1]

NAFLD

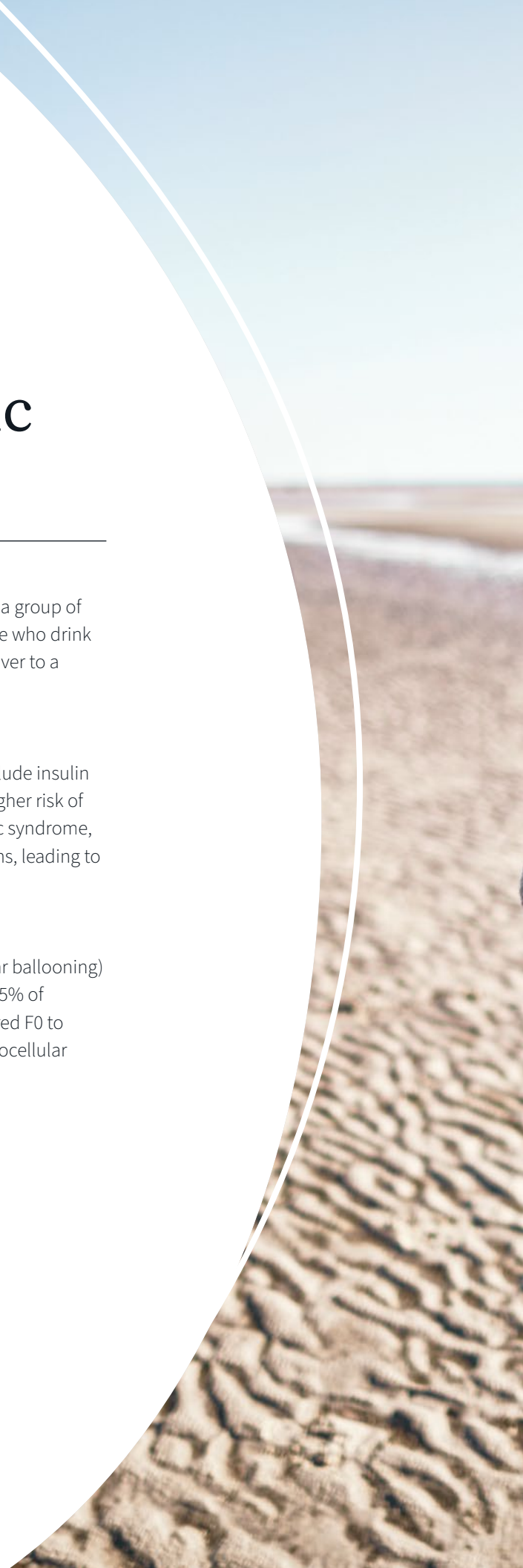
NAFLD patients with obesity and features of the metabolic syndrome that include insulin resistance, type 2 diabetes mellitus, hypertension and dyslipidemia have a higher risk of progression to NASH. Not all patients have all manifestations of the metabolic syndrome, however. With the development of NASH, the cardio-metabolic profile worsens, leading to a higher risk of cardiovascular events and death.[1,2]

NASH

NASH is a chronic liver disease characterized by liver cell injury (hepatocellular ballooning) and inflammation as a result of fatty accumulation (steatosis) seen in at least 5% of hepatocytes. This leads to liver scarring and the development of fibrosis (scored F0 to F4). As fibrosis worsens, liver-related morbidity (including cirrhosis and hepatocellular carcinoma) and mortality increase.[2]

80+ million

Number of people in the United States living with NAFLD[7]



NAFLD patients with obesity and features of the metabolic syndrome that include insulin resistance, type 2 diabetes mellitus, hypertension and dyslipidemia have a higher risk of progression to NASH.

Identification of patients at higher risk of NAFLD, NASH and advanced fibrosis is the first step in optimizing patient management and therapy.

Symptoms of NASH

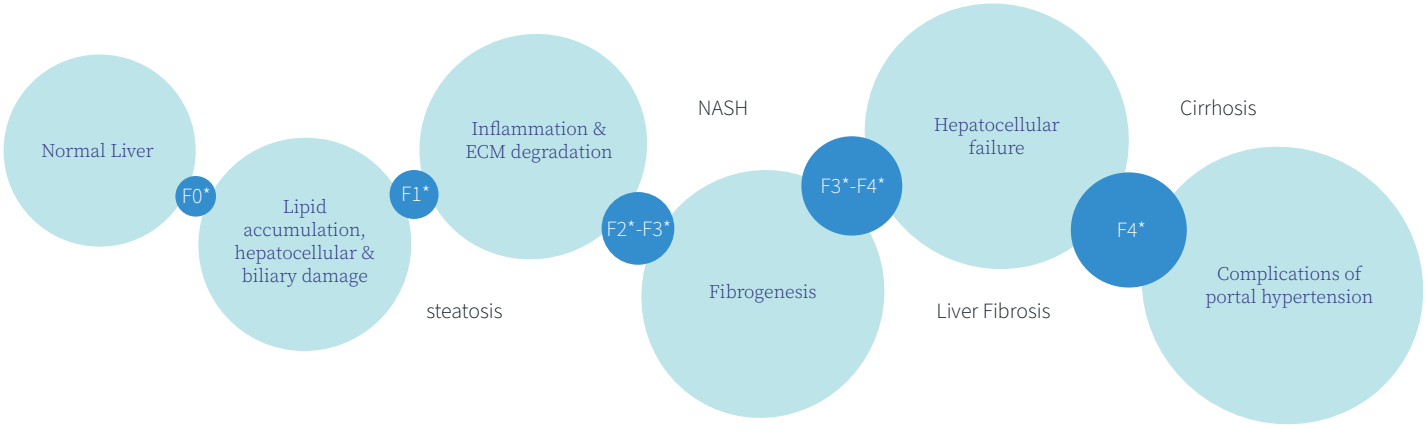
The symptoms of NASH may be very non-specific and can include fatigue, daytime tiredness, or abdominal pain early in the disease. It is usually discovered incidentally due to elevated liver enzymes, abnormal imaging studies or surgery. As cirrhosis advances, NASH-specific symptoms are more commonly manifested.[2]

Typically, most people who develop NASH are between 40 and 50 years old, and have one or more of the following health concerns: obesity; insulin resistance and type 2 diabetes; high cholesterol and triglycerides; metabolic syndrome. On the other hand, it is possible for individuals with none of these risk factors to develop NASH.[3]

Prevalence of NAFLD

The prevalence of NAFLD in the United States is reported to be between 10% and 30%[5], and the pooled overall global prevalence of NAFLD diagnosed by imaging was estimated to be greater than 25%.[6] However, the exact prevalence of NAFLD and NASH in an adult population remains difficult to assess due to the lack of a cost-effective and widely available, minimally-invasive diagnostic test, and to the absence of specific symptoms before end-stages. There are many medications in development for the treatment of NASH; diet, lifestyle modifications and exercise are current recommendations.[7]

NASH Progression



*NASH Clinical Research Network (CRN) Scoring System

It is estimated that more than 16 million people in the United States are living with NASH, and the prevalence of NASH will increase by 63% by the year 2030.[1]

At Labcorp, we believe proper testing can help slow the trends by helping identify those at risk of developing NAFLD and NASH.

APRI (385375)
The AST to Platelet Ratio Index (APRI) assay is reported to be a simple, noninvasive, and readily available laboratory test index that can stratify patients with HCV and NAFLD who are at high or low risk for significant fibrosis and cirrhosis with high degree of accuracy. Results from the APRI test include AST, platelet count and the APRI score.

Enhanced Liver Fibrosis (550659)
The Enhanced Liver Fibrosis (ELF™) blood test is a simple, accurate, non-invasive test that provides a numeric score for use in patients known to have advanced liver fibrosis. It is indicated as a prognostic marker in conjunction with other laboratory findings and clinical assessments in patients with advanced fibrosis (F3 or F4) due to NASH in order to assess the likelihood of progression to cirrhosis and liver-related clinical events.[8]

FIB-4 (403604)
The FIB-4 index is reported to be a simple, accurate, noninvasive, and readily available laboratory test index that can help in evaluation of patients with HCV and NAFLD for the presence of liver fibrosis, and the indication for liver biopsy, and other liver-related complications. Results from the FIB-4 test include ALT, AST, platelet count and the FIB-4 score.

FIB-4 With Reflex to Enhanced Liver Fibrosis (ELF) (402175)
See individual tests descriptions.

FIB-4 With Reflex to NASH FibroSure® Plus (402146)
See individual tests descriptions.

Liver Fibrosis Risk Profile With Hepatic Function Panel, Complete Blood Count (CBC) With Differential, FIB-4, and APRI (402145)
This profile is intended for use in screening patients suspected to be at risk for liver fibrosis. AST to Platelet Ratio Index (APRI) is reported to be a simple, noninvasive, and readily available laboratory test index that can stratify patients with HCV and Non-Alcoholic Fatty Liver Disease (NAFLD) who are at high or low risk for significant fibrosis and cirrhosis with high degree of accuracy. FIB-4 index is reported to be a simple, accurate, noninvasive, and readily available laboratory test index that can help in evaluation of patients with HCV and Non-Alcoholic Fatty Liver Disease (NAFLD) for the presence of liver fibrosis indication for liver biopsy, and other liver-related complications.

NASHnext™ (504960)
Utilizing NIS4™ technology, NASHnext is a blood-based diagnostic test that quantitatively measures four independent biomarkers to produce a score that identifies, among patients with metabolic factors, those with at-risk NASH, who are at higher risk of disease progression.

NASH FibroSure® (550140)
This noninvasive assessment of liver status in patients with NAFLD provides quantitative results of 10 biochemicals in combination with age, gender, height, and weight. These factors are analyzed using a computational algorithm to provide a quantitative surrogate marker (0.0-1.0) of liver fibrosis (Metavir F0-F4), hepatic steatosis (0.0-1.0, S0-S3), and NASH (0.0-0.75, N0-N2). The absence of steatosis (S<0.38) precludes the diagnosis of NASH.

NASH FibroSure® Plus (550960)
NASH FibroSure® Plus offers a more streamlined testing process than NASH FibroSure: BMI is no longer included in the calculation, eliminating one step for providers.

NAFLD and NASH Related Tests

Test Name	Test No.
NASH	
AST and Platelets with APRI	**385375**
Enhanced Liver Fibrosis (ELF™)	**550659**
FIB-4	**403604**
FIB-4 With Reflex to Enhanced Liver Fibrosis (ELF)	**402175**
FIB-4 With Reflex to NASH FibroSure® Plus	**402146**
Liver Fibrosis Risk Profile with Hepatic Function Panel, Complete Blood Count (CBC) With Differential, FIB-4, and APRI	**402145**
NASHnext™	**504960**
NASH FibroSure®	**550140**
NASH FibroSure® Plus	**550960**
Non-Alcoholic Fatty Liver Disease Advanced Fibrosis Rule-Out Cascade	**402205**
Risk of Cardiovascular Disease and Type 2 Diabetes	
Glucose, Plasma	**001818**
Hemoglobin (Hb) A1c	**001453**
Insulin	**004333**
Lipid Panel Plus ApoB	**123544**
Lipid Panel Plus Diabetes Risk Index	**123525**
Lipid Panel Plus Inflammation	**123510**
Lipid Panel Plus Inflammation and Diabetes Risk Index	**123559**
Lipid Panel Plus Inflammation, Diabetes Risk Index and Apo B	**123567**
NMR LipoProfile® With Insulin Resistance Markers Without Lipids	**123497**
NMR LipoProfile® With Lipids and Insulin Resistance Markers	**123638**
Liver Related Markers	
α2-Macroglobulin, Quantitative	**122135**
Alanine Aminotransferase (ALT/SGPT)	**001545**
Albumin	**001081**
Alkaline Phosphatase	**001107**
Aspartate Aminotransferase (AST/SGOT)	**001123**
Bile Acids	**010330**
Lactic Acid Dehydrogenase (LD)	**001115**
Protein, Total	**001073**
ASH	
ASH FibroSure®	**550180**
Ethyl Glucuronide/Ethyl Sulfate (EtG/EtS), Screen and Confirmation, Urine	**737610**
Hepatitis	
Acute Viral Hepatitis (HAV, HBV, HCV)	**144000**
Hepatitis A Virus (HAV) Antibody, Total	**006726**
Hepatitis A Antibody, IgM	**006734**

Test Name	Test No.
Hepatitis B Virus (HBV) Screening and Diagnosis	**144473**
Hepatitis B Core Antibody, Total	**006718**
Hepatitis B Surface Antibody, Qualitative	**006395**
Hepatitis B Surface Antigen (HBsAg) Screen, Qualitative	**006510**
Hepatitis B Surface Antigen, Quantitative, Monitor	**007130**
Hepatitis B Virus (HBV) Genotype	**551710**
Hepatitis B Virus (HBV) Genotyping Plus Drug Resistance	**551750**
Hepatitis B Virus (HBV), Quantitative, DNA Real-time PCR, (Nongraphical)	**551610**
Hepatitis C Virus (HCV) Antibody With Reflex to Quantitative Real-time PCR	**144050**
Hepatitis C Virus (HCV) FibroSure®	**550123**
Hepatitis C Virus (HCV) GenoSure® NS3 / 4A	**550540**
Hepatitis C Virus (HCV) Genotype 3 NS5A Drug Resistance Assay	**550603**
Hepatitis C Virus (HCV) Genotyping, Nonreflex	**550475**
Hepatitis C Virus (HCV) NS5A Drug Resistance Assay	**550325**
Hepatitis C Virus (HCV) NS5B Drug Resistance Assay	**550505**
Hepatitis C Virus (HCV), Quantitative, Real-time PCR (Graphical)	**550070**
Hepatitis C Virus (HCV), Quantitative, Real-time PCR (Nongraphical)	**550080**
Hepatitis C Virus (HCV), Quantitative, RNA PCR (Graphical) With Reflex to Genotyping	**550100**
Hepatitis C Virus (HCV), Quantitative, RNA PCR (Nongraphical) With Reflex to Genotyping	**550090**
Other	
α-Fetoprotein (AFP), Tumor Marker	**002253**
α-Fetoprotein (AFP), Tumor Marker (Serial Monitor)	**480012**
α-Fetoprotein (AFP) With AFP-L3%, serum	**141300**
α1-Antitrypsin, Serum (preferred) or plasma	**001982**
α1-Antitrypsin Deficiency, DNA Analysis	**511881**
α1-Antitrypsin Phenotyping, Serum	**095653**
γ-Glutamyl Transferase (GGT)	**001958**
Actin (Smooth Muscle) Antibody (ASMA)	**006643**
Ammonia, Plasma	**007054**
Bilirubin, Total and Direct	**001214**
Ceruloplasmin	**001560**
Copper, Serum or Plasma	**001586**
Copper, Urine	**003343**
Hereditary Hemochromatosis, DNA Analysis	**511345**
Liver-Kidney Microsomal (LKM) Antibodies	**163980**
Mitochondrial (M2) Antibody	**006650**
Soluble Liver Antigen (SLA) IgG Antibody	**007441**
Thyroid Peroxidase (TPO) Antibodies	**006668**

Power of the Combined

Labcorp and Labcorp Drug Development working to bring NASH technologies to the forefront

Superior testing options with NASHnext™, NASH FibroSure®, NAFLD cascade, and more through Labcorp

- 15 NAFLD/NASH studies in 5 years, with 4 global phase 3 studies in progress at Labcorp Drug Development
- 4,000+ biopsy-confirmed patients recruited by Labcorp Drug Development, plus metrics on 700+ sites across 28 countries
- 31 NAFLD/NASH and NASH cirrhosis studies currently being conducted in our labs as of 2019

Drug development leadership & medical testing expertise makes Labcorp Drug Development & Labcorp your choice for NASH collaboration

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8. ADVIA Centaur® Enhanced Liver Fibrosis (ELF) [package insert]. Tarrytown, NY. Siemens Healthcare Diagnostics Inc. Rev. 01, 2021-08.

For more information about NASH-NAFLD and how it can benefit your patients, visit **Labcorp.com/NASH**

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