

Non-Alcoholic Fatty Liver Disease

Non-alcoholic fatty liver disease (NAFLD) is the [most prevalent liver disease in human history](#) with estimates indicating it affects almost two billion people globally. It is expected to grow in the coming decades, compromising individual health, burdening health care systems, and causing substantial economic and well-being losses.

EMPLOYERS:

If you have a diabetes problem, you most likely have a NAFLD problem!

This Action Brief includes recommendations on ways purchasers can combat this silent epidemic.



Look for this symbol for employer quotes on the challenges and opportunities to support their efforts.

Direct medical costs of NAFLD in the U.S. are estimated at \$103 billion annually. Because of the close correlation with diabetes and pre-diabetes, employer costs related to NAFLD are expected to increase proportionately with the growing diabetes epidemic.

The Silent Epidemic: Why Employers Should Care

Liver disease is a silent epidemic that affects millions of Americans and imposes significant financial burdens on the U.S. health care system. Sixty percent (60%) of all liver disease is caused by NAFLD where fat builds up in the liver. This condition is an increasing contributor to growing liver-related morbidity and mortality. When NAFLD is present, the following

comorbidities are more likely to develop:

- Overweight or obesity, especially abdominal obesity
- Type 2 diabetes or prediabetes (elevated blood sugar); high levels of triglycerides and LDL cholesterol; low levels of HDL cholesterol
- Metabolic syndrome

NAFLD at-a-Glance

- Build-up of fat in the liver that can lead to inflammation and scarring; in severe cases can lead to cirrhosis and liver cancer.
- In early stages, there are **no symptoms, pain or discomfort**.
- Most common cause of chronic liver disease in the U.S.; **estimated that 100 million Americans** are affected.
- Impacts large portion of U.S. adult population and growing with the obesity and diabetes epidemics.
- 22% of Americans have NAFLD; **primary risk factors** include being over the age of 50 and/or



with metabolic syndrome; NAFLD is present in:

- ▶ 80% to 90% of adults with obesity
- ▶ 50% to 70% of adults with type 2 diabetes
- ▶ Up to 90% of adults with hyperlipidemia

- **Doubles likelihood** of progressing from pre-diabetes to diabetes.

- Because it is **often diagnosed at an older age**, liver failure can be the first sign of NAFLD-related cirrhosis in 38% to 45% of cases.

Progression of NAFLD

Approximately 20% of those with NAFLD have or will progress to non-alcoholic steatohepatitis (NASH), a type of NAFLD that [causes inflammation and liver damage, along with elevated fat in the liver](#). NASH can lead to cancer and liver failure, and is the most [rapidly increasing](#) indication for liver transplant. With NASH, [no medicine can fully reverse fat buildup in the liver](#). For people with NASH, it is important to control risk factors that contribute to the disease.

By 2030, it is estimated that [27% of people with NAFLD](#) will develop NASH.



“We had a year over year increase in liver disease of 25% (from 33% to 41%). It is an alarming trend that we have to keep monitoring, and with metabolic syndrome implications, addressing NAFLD has become a bigger priority at our organization.”

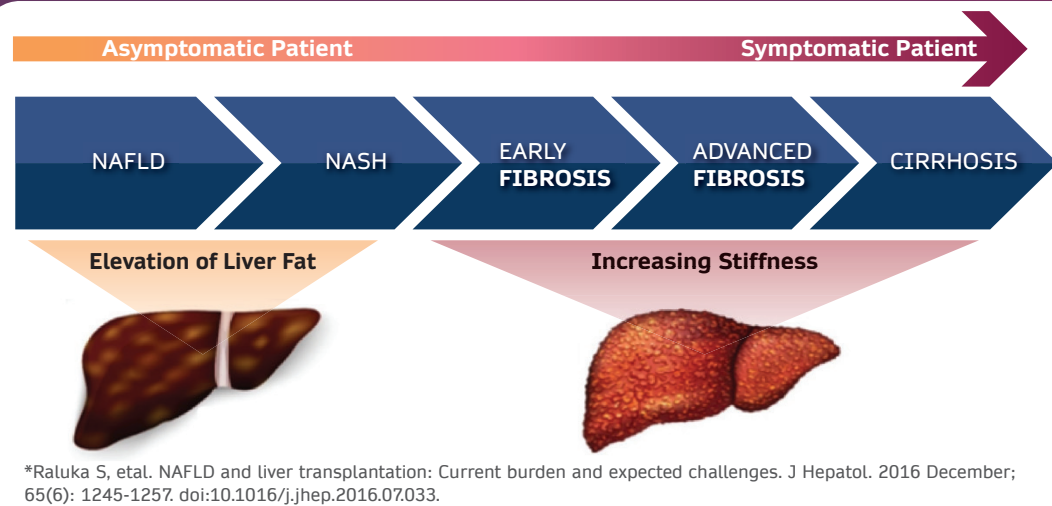
NAFLD or NASH

- Patient has fat but no inflammation or tissue damage = NAFLD
- Patient has fat, inflammation and liver damage = NASH
- Patient has a type of scar tissue in the liver called fibrosis = may be developing cirrhosis

Because NAFLD is asymptomatic, definitive assessment, diagnosis and ongoing monitoring are critical to diagnose it in its early stages. Yet, in the absence of an evidence-based screening strategy and effective

treatments, many individuals remain undiagnosed. As a result, patients with NASH often present at late clinical stages with cirrhosis or liver cancer.

Fortunately, a growing number of newer and evolving technologies are available to help with early detection, monitoring and management of NAFLD/NASH. This is especially important given the significant number of high-cost specialty drugs in the pipeline.



Focus on T2DM and NAFLD: “Bidirectional Association”

The [American Diabetes Association \(ADA\) “Standards of Medical Care in Diabetes”](#) includes the current clinical practice recommendations and is intended to provide the components of diabetes care, general treatment goals and guidelines, and tools to



evaluate quality of care. These recommendations indicate:

- Diabetes is associated with the development NAFLD, including its more severe manifestations of NASH, liver fibrosis, cirrhosis and hepatocellular carcinoma (cancer).
- Elevations of liver enzymes are associated with higher BMI, waist circumference and triglyceride levels, and lower HDL cholesterol levels.
- Noninvasive tests, such as [liver elastography](#) or [fibrosis biomarkers](#) may be used to assess the risk of fibrosis.



ADA Recommendations:

Patients with type 2 diabetes or prediabetes and elevated liver enzymes (ALT) or fatty liver on ultrasound should be evaluated for presence of nonalcoholic steatohepatitis and liver fibrosis.



New guidelines from the U.S. Preventive Services Task Force ([USPSTF](#)) recommend screening adults aged 35 to 70 years who are overweight or have obesity for prediabetes and type 2 diabetes, and offer preventive interventions. There is hope that USPSTF will recognize the need to include references to NAFLD and NASH in their [future guidelines](#).

Employer Economic Impacts

- Largest increases in health care utilization were represented by liver biopsies, imaging and hospitalizations; for the commercial population, [the annual cost of NAFLD](#) is \$9,062 for a new diagnosis and \$5,363 for long term management, versus \$4,111 per matched control. Fatty liver disease is a diagnosis of exclusion so the cost of diagnosis can be very high.
- [Recent analysis](#) of health care expenditures showed long-term cumulative costs for a patient with NAFLD/NASH was 80% higher than someone of a comparable age with similar metabolic comorbidities.
- Indirect costs include impacts on [worker productivity](#); 53% of people with mild NASH reported work-related problems or sick leave – this was true for 74% of people with late-stage disease.
- [Cumulative 5-year health care costs](#) of an individual with NAFLD/NASH are estimated to be more than \$95,000; an individual with cirrhosis is estimated to cost \$134,000, and liver cancer costs \$331,000.

*The Good News!
If NAFLD
has not yet
advanced,
it can be reversed.*



Diagnosis & Treatment Options

NAFLD is not just a disease seen by [hepatologists](#). More health care providers, including [endocrinologists](#) and primary care physicians (PCPs) caring for patients with type 2 diabetes, are paying attention to liver disease as it makes managing diabetes more challenging. Early identification and intervention for NAFLD and NASH can significantly improve outcomes and reduce employer health care costs.

An overview of current and new diagnostic and treatment options include:

Lifestyle Modification

The best way to reduce NAFLD disease progression is through lifestyle modification and behavior change programs, including nutrition, physical activity and behavioral health components. These lifestyle changes can control or reverse the fat buildup in the liver. They are traditionally offered through employer-based wellness programs, point solution vendors, carriers, EAPs and/or community organizations. The most successful programs are evidence-based and focus on behavioral lifestyle intervention.

Diagnostic Testing

The prevalence of NAFLD is [difficult to measure](#) due to its lack of consistent diagnostic criteria. And, because there are no symptoms in the early stages, the disease is not

“We need to not only consider onsite wellness screenings, but integrate liver health into executive physicals, education for our onsite clinic physicians and even mobile screening units.”



easily recognized by most specialists and physicians.

When liver disease is suspected, the primary care doctor typically sends the patient to a liver specialist who conducts:

- Medical history and physical exam
- Blood work to check for increased levels (abnormal) of liver enzymes
- Imaging such as a CT scan, ultrasound or MRI

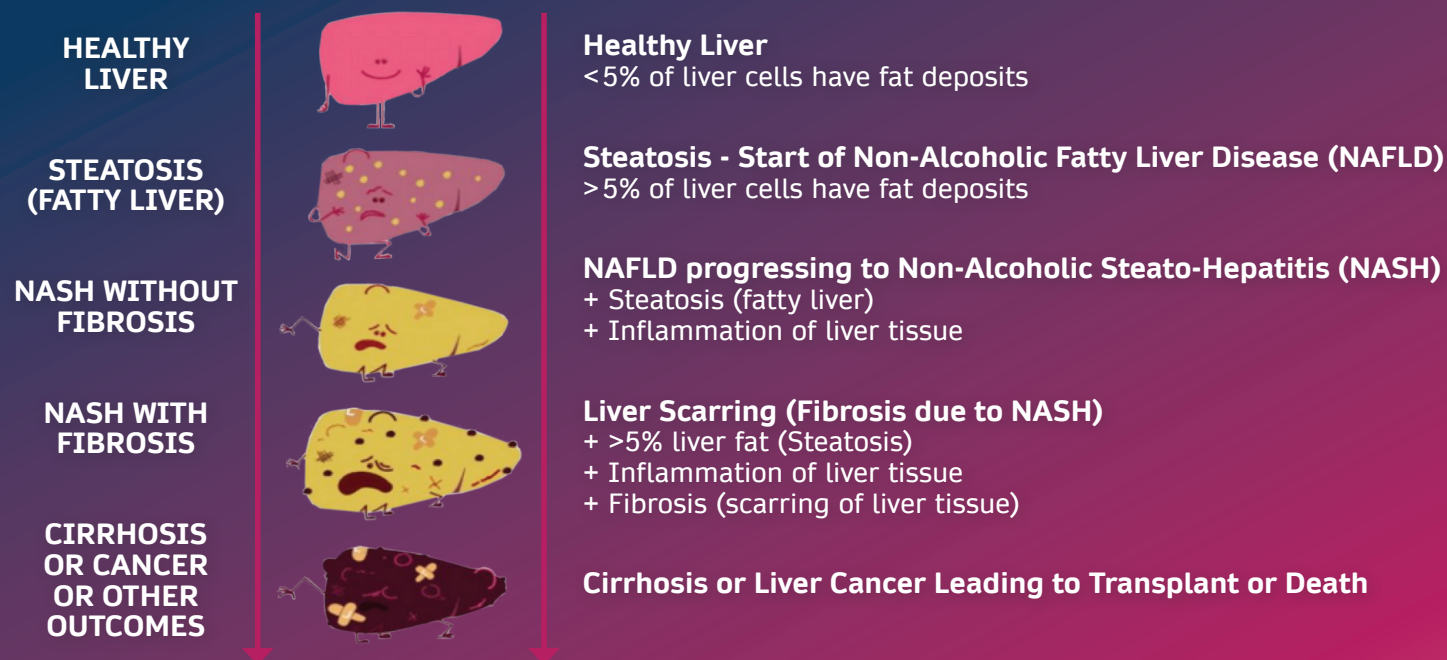
Challenges with Standard Tests and Liver Biopsies

A typical blood panel that looks at liver enzymes can be a good marker. However, with advanced fibrosis or cirrhosis the patient may not have enough liver integrity to create elevated liver enzymes.

Traditional diagnostics such as liver enzyme tests and imaging do not measure how much fat, stiffness or fibrosis there is in the liver, affecting the ability to determine if the patient is at elevated risk or to identify the disease in its early stages.

For those who already have NAFLD/NASH, the standard test is a liver biopsy (an invasive test that involves removing a piece of liver tissue for testing). The procedure is expensive, often unnecessary, and can pose certain risks such as pain, infection and bleeding.

NAFLD: Disease Progression Resulting from Poor Diet and Inadequate Exercise



Adopted From: Features, Diagnosis & Treatment of NAFLD: Torres, Williams & Harrison; Clinical Gastroenterology Hepatology. 2012;10:837-858;
<https://www.ncbi.nlm.nih.gov/pubmed/22446927>

Specialty Drugs in the Pipeline

Increased awareness of NAFLD has led to a robust pipeline for over 50 new FDA-approved medications. One therapy is expected to be priced at **\$10K to \$18K** per patient per year (anticipated to launch soon). This category of liver drug therapies will likely start hitting the market between 2023 and 2025 and is forecasted to be a **\$20 billion to \$35 billion** industry.



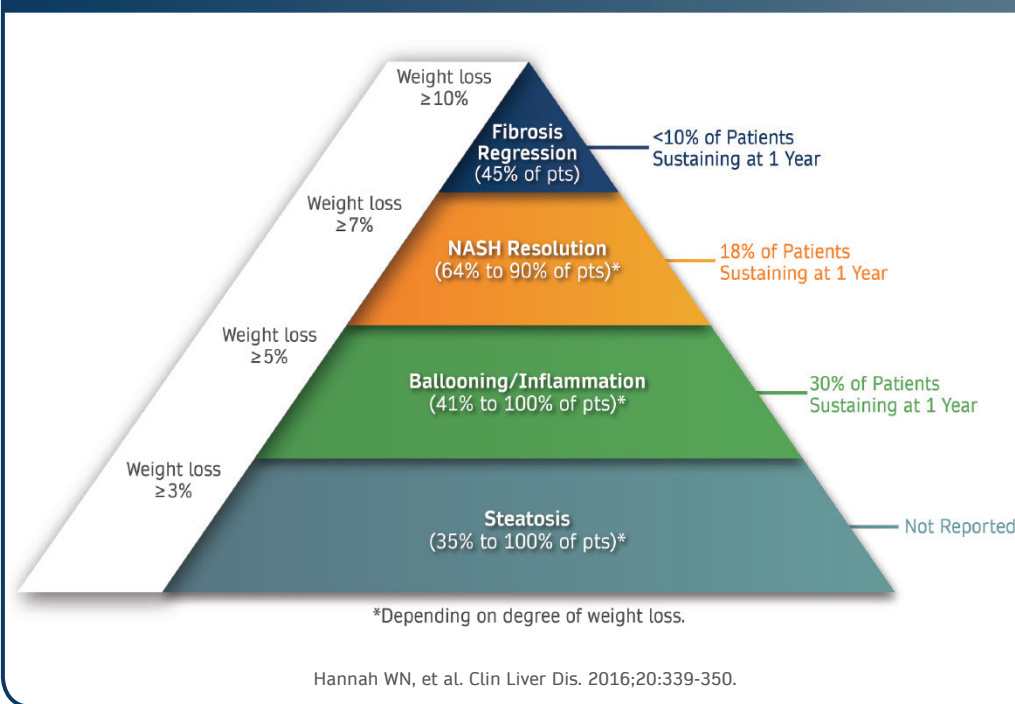
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Newer Testing Options

Because fibrosis is a condition that reduces blood flow to and inside the liver, buildup of scar tissue results. Left untreated, fibrosis can lead to serious problems in the liver, including [cirrhosis](#), [liver](#)

[cancer](#) and liver failure. But early diagnosis and treatment can reduce or even reverse the effects of fibrosis. Newer diagnostic liver assessment tests are non-invasive and focused on early detection, monitoring and management of NAFLD/NASH.

Weight Loss Can Reduce Fatty Liver Disease



Healthy Liver

NAFLD

NASH

Cirrhosis



[Elastography tests](#) are conducted during a clinical exam to measure the stiffness of the liver - the stiffer the liver, the more fibrosis is present. The results range from no liver scarring to mild, moderate, or advanced scarring with advanced scarring known as cirrhosis. A health care provider may order additional tests to confirm the diagnosis. The two types include:

- **Ultrasound elastography** uses sound waves to measure the stiffness of liver tissue – a sign of fibrosis. This testing may be used in place of a liver biopsy. Other

names include liver elastography, transient elastography, FibroScan, MR elastography.

- **MRE (magnetic resonance elastography)** combines ultrasound technology with magnetic resonance imaging ([MRI](#)). Procedure uses powerful magnets and radio waves to create images of organs and structures inside the body. A computer program creates a visual map that shows liver stiffness.

Liver elastography tests can serve as an important step in addressing some of the wasteful practices that result from unnecessary specialist referrals, some

“It’s one thing to tell a patient they have liver disease and should watch their diet and lifestyle. It’s another thing to show them a liver score and where they fall on the scale – it’s a big eye opener.”



“We need to make NAFLD testing part of the standard protocol with our health assessments. If a member is diagnosed with diabetes, they should get this test. As an employer, we have no problem pointing members to a provider in the community that offers this type of testing.”

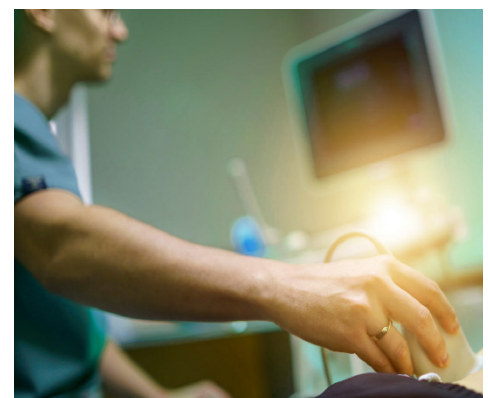
Commentary: Mark Fendrick, M.D., co-editor in chief, AJMC, professor of Medicine, School of Medicine, professor of Health Management and Policy, School of Public Health, and director, Center for Value-Based Insurance Design, University of Michigan

“Scoring systems such as the Fibrosis-4 ([FIB-4](#)) index and NAFLD fibrosis score ([NFS](#)) are validated methods to risk stratify using low-cost and routine laboratory tests with high negative predictive value for advanced liver fibrosis. For those individuals who require further work-up, [VCTE](#) (Vibration-Controlled Transient Elastography) can provide additional clinical information.

....VCTE is superior to routine liver ultrasound for the objective assessment of liver scarring and fatty infiltration. VCTE offers excellent negative predictive value and fair positive predictive value.”

tests and high-cost procedures. These tests will play a key role when medications for treating NAFLD and NASH reach the market (see below).

Those diagnosed with mild to moderate fibrosis, may be able to take steps to stop further scarring and sometimes even improve the condition of the liver. If no action is taken, more scar tissue will build up in the liver which can lead to cirrhosis. Sometimes, the only treatment for advanced cirrhosis is a [liver transplant](#).



“We should start with a liver enzyme test as a first step and then graduate to newer treatment options BEFORE we get to more expensive and invasive tests, procedures and treatments.”

Employer Action Steps

Educate Health Care Partners (e.g. Carriers, TPAs, PBMs, Wellness/Wellbeing Vendors) to:

- Understand the prevalence, importance and impacts of NAFLD and NASH.
- Cover new diagnostic testing options such as elastography tests, and monitor CPT codes to make sure they are being prescribed and used.
- Recognize how certain unnecessary procedures and tests can significantly increase employer costs and work with partners to address this.
- Start a conversation with your PBM about how new drug therapies in the pipeline will impact costs to the plan and what guidelines need to be put into place to control spend when they come to market.
- Understand partner strategies for identifying members at risk.
- Ensure vendor solutions for lifestyle/behavior modification, chronic disease management and advocacy/navigation focus on prediabetes, type 2 diabetes and obesity.



“All of us have diabetes management programs that include standards of care. We must use this same approach for NAFLD & NASH and we need our partners to know what the standards of care are and use them.”



Build Liver Health Monitoring into Existing Programs and Benefits:

- Integrate liver health monitoring into annual wellness visits, health screenings and executive physicals.
- Direct members to clinical facilities where new testing options are provided.
- Make sure on-site/near-site health clinic experts and clinicians are knowledgeable about NAFLD and include a elastography tests as a standard of care.
- Ensure partners are covering these tests and that appropriate network providers are making them available.
- Provide partners with educational tools to use during office and telehealth visits and guide patients to best practice treatments.
- Create a value-based benefits design with low or no copays for liver health monitoring, especially for people with diabetes, obesity and/or multiple comorbidities.
- Work with centers of excellence to implement programs to address liver health.
- Educate members to understand the impact of lifestyle on liver health; steer at risk members to appropriate programs and interventions.
- Screen adults aged 35 to 70 years who are overweight or have obesity for prediabetes and type 2 diabetes and offer preventive interventions.
- Focus on cardiovascular risk reduction and continue to manage hypertension and dyslipidemia (e.g. cholesterol, triglycerides, HDL); offer support for smoking cessation.

“We need to educate the consumer because this is not on their radar unless their doctor has talked to them about it.”



About MBGH

MBGH is one of the nation's leading and largest non-profit employer coalitions. Members are represented by human resources and health benefit professionals for over 140 mid, large and jumbo self-insured public and private companies who provide health benefits for more than 4 million lives, with employer members spending over \$12 billion annual on health care. Since 1980, members have used their collective voice to serve as catalysts to improve the cost, quality and safety of health care benefits.

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