Two-Fold Epidemic:

Fatty Liver Disease and Obesity Demand Proactive Steps, Earlier Identification of Liver Damage

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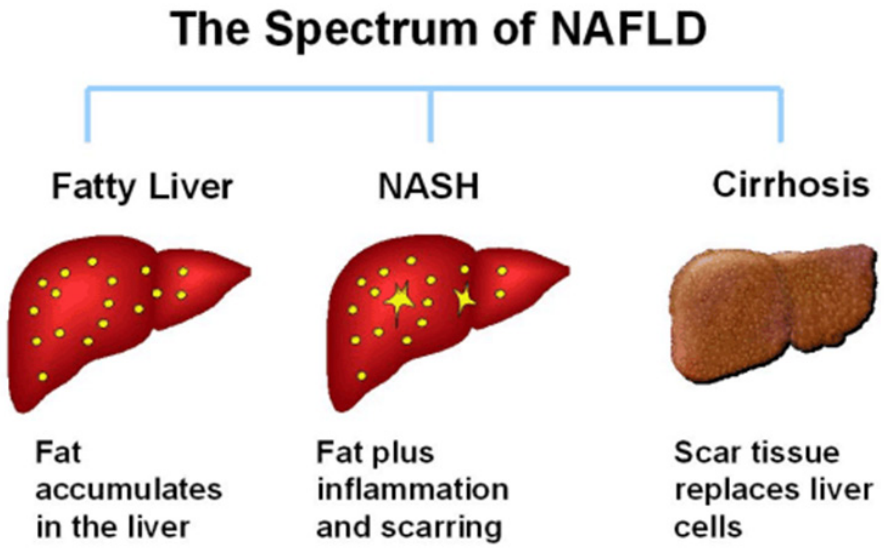
The alarming rise in adult obesity rates in the United States and worldwide has led to more people experiencing liver damage and associated health issues. For context, in 2000, 30.5% of American adults had obesity, meaning they had a body mass index of 30 or higher. That rate increased through 2015-2016, helping to fuel related health issues like diabetes, cardiovascular disease and some cancers. Recent data shows that the obesity rate reached 42.4% in 2017-2018 – surpassing 40% for the first time.[1]

The impact of obesity on vital organs can be devastating, especially on the liver, causing insulin resistance that leads to buildup of blood sugar and increases the amount of free fatty acids circulating in the blood and inside the liver cells. This buildup of fat is very common in those with Type 2 diabetes, and increases the risk of liver fibrosis, cirrhosis, liver cancer and death.

It also leads to non-alcoholic fatty liver disease (NAFLD), which affects roughly 100 million Americans and costs the United States healthcare system $32 billion annually.[2] In a recent retrospective analysis among Medicare Advantage plans, the annual cost of NAFLD was $9,062 for a new diagnosis and $5,363 for long term management versus $4,111 per matched control.[3]

It should come as no surprise that the prevalence of NAFLD mirrors the rising trend of obesity in the United States. Costs per patient and overall costs per year are the result of inpatient hospitalization and outpatient appointments, emergency department visits, organ transplantation, medical procedures or new diagnoses, new medications or changes to existing medications and mortality.



Source[4]

NAFLD is just beginning to gain prominence on the public radar as discussions about its alarming rise across populations is generating attention among providers and payers. These two groups are well positioned to battle this epidemic and play a role in educating U.S. citizens about the dangers of NAFLD and its link to obesity. With this type of interest and support, they can encourage lifestyle changes and identify ways to easily screen for liver disease before it becomes a serious health threat. The good news is that NAFLD is reversible if caught in the early stages and accompanied by lifestyle changes.

This paper highlights key aspects of this healthcare crisis for providers, payers and patients. It also articulates the value of an innovative, non-invasive diagnostic tool that is cost-effective and provides rapid, consistent results to enable heath care professionals to make the most informed treatment decisions, while also ruling out the need for an expensive liver needle biopsy or other invasive testing.

Obesity is a Chronic Disease

Obesity is not simply a matter of over-eating, but rather a complex disease that involves an excessive amount of body fat. To overcome the stigma of obesity, it's important to view this disease as a complex medical issue that increases the risk of heart disease, diabetes, high blood pressure and certain cancers. Given its overwhelming prevalence–1 in 6 U.S. adults–obesity is now recognized as a chronic disease by several organizations, including the American Medical Association.

The Centers for Disease Control and Prevention (CDC) defines chronic disease as conditions that last one year or more and require ongoing medical attention or limit activities of daily living, or both.[5] Of the $3.3 trillion spent annually on medical care for chronic conditions, obesity alone is associated with $1.4 trillion.[6]

Challenges Across the Spectrum of Care

Providers

Too often, patients with obesity lack the health literacy and diagnoses necessary to motivate them to access long-term care solutions. One study found that of the 70% of patients who had spoken with their healthcare providers about their weight, only 55% received a formal diagnosis for obesity, and only 24% have been referred to weight loss follow-up care.[7] These findings suggest that clinicians need to leverage better patient-provider communication surrounding a patient's health status.[8]

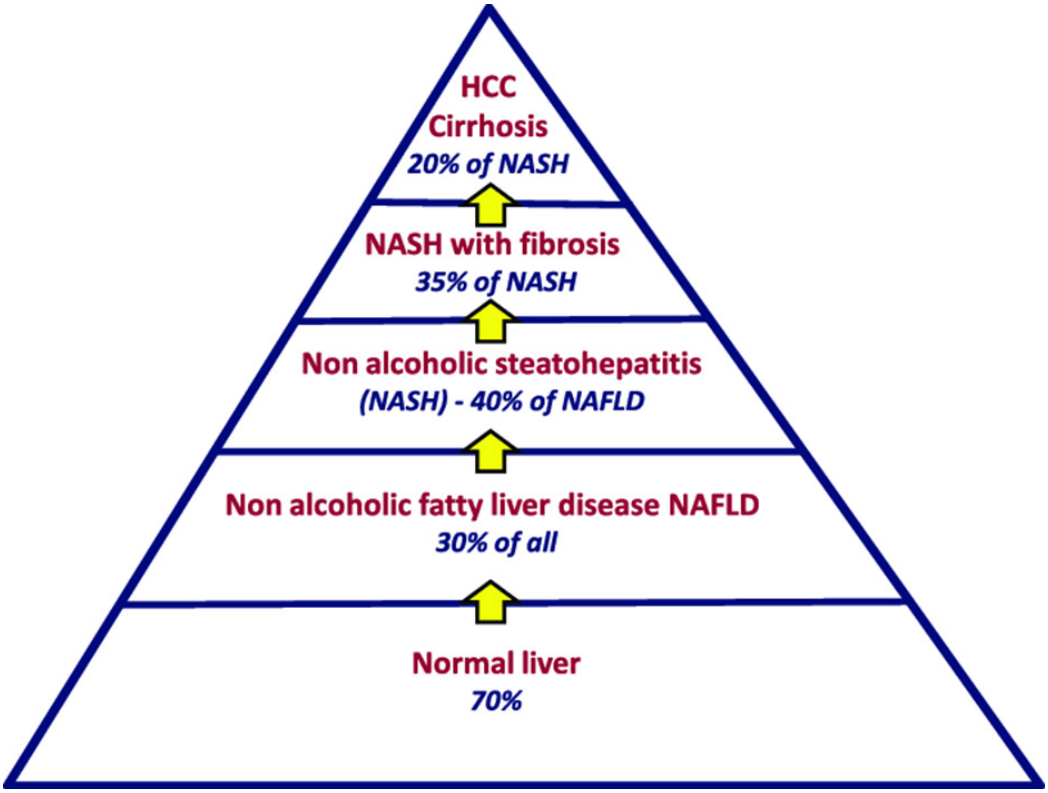
Physicians can order a blood test to look for liver proteins released after a liver cell dies, which may suggest inflammation. Elevated liver enzymes alone do not correlate with NASH and moreover, the upper limits of normal cutoffs for liver function testing by the major labs may be 50% higher than recommended by the American Gastroenterology Society.[9]

Today's gold standard remains a liver sample, allowing doctors to see signs of scar tissue and ballooning under a microscope to determine how far the disease has progressed. This method, however, has been brought into question not only for its invasiveness and risk, but also for its inaccuracy.

Payers

According to a large-scale survey, 70% of employers believe their wellness programs are valuable to employees, but only 17% of people with obesity believe their employers' wellness programs are effective for them.[10]

Broader costs to consider, especially for employers, include absenteeism and lost productivity. Interventions that are convenient, credible and supported by evidence can increase engagement and results, keeping in mind that coverage of services does not automatically lead to utilization or mean quality of care.[11]



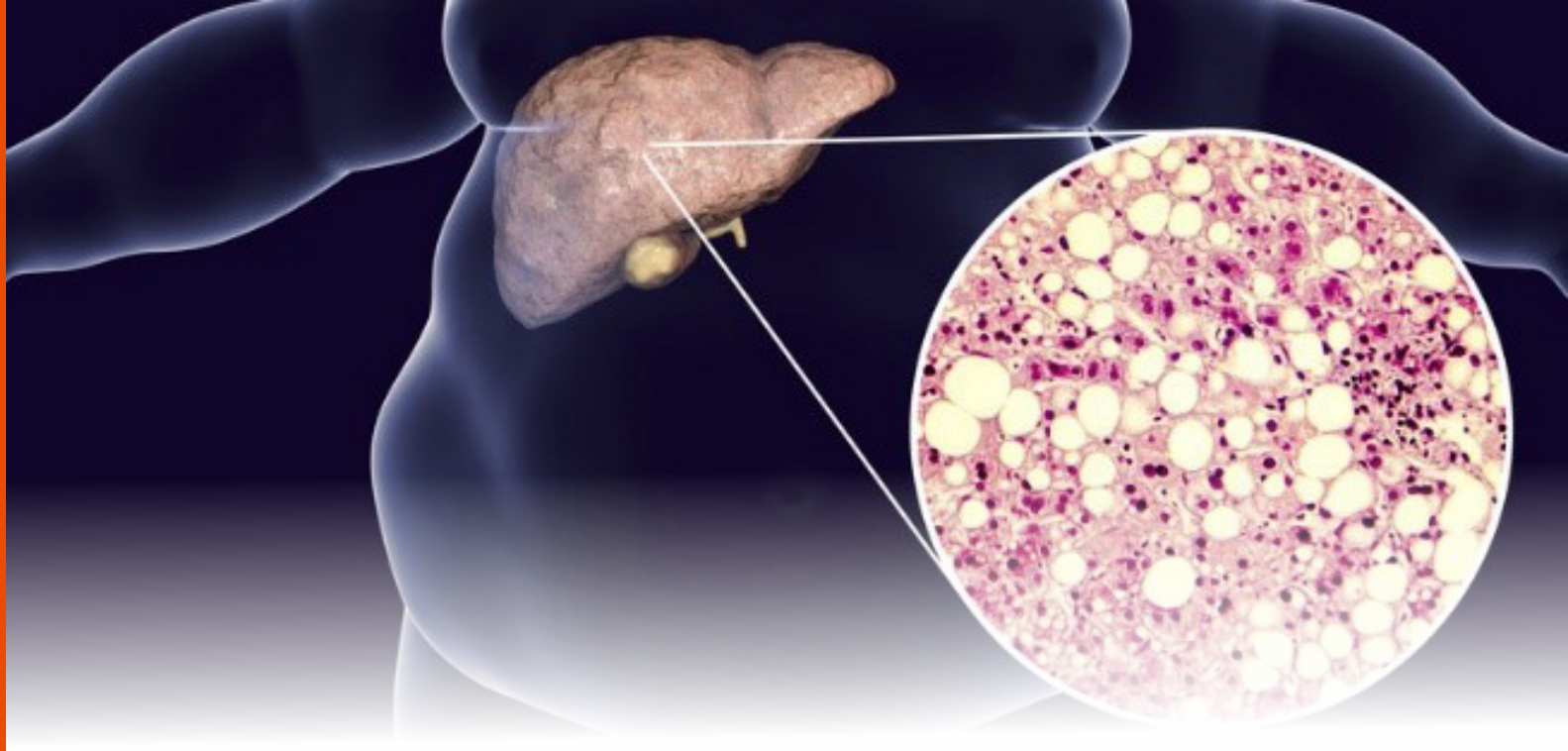
Epidemiology of, NAFLD, NASH, cirrhosis and hepatocellular carcinoma. Based on Refs. [1-5, 13]. NAFLD = non-alcoholic fatty liver disease, NASH = non-alcoholic steatohepatitis, HCC = hepatocellular carcinoma.

Source[12]

The Obesity and NAFLD Connection

Having some fat in the liver is normal, but when fat accounts for more than five percent of the organ's weight, it becomes dangerous. Alcoholism has long been the best-known cause of fatty liver, but most cases are considered a metabolic problem — an issue with the way the body processes and stores food.

With NAFLD, the problem starts with the buildup of excess fats. The liver normally breaks down fats into smaller pieces, which are then transported and stored in white adipose tissue in the cheeks, gut and thighs. Once those reservoirs fill, excess fat or sugars turn into fat, collect in the muscles, heart and liver, and develop into the first stage of NAFLD, called steatosis. When the liver cells balloon with fat, it turns the liver yellow, greasy and toxic.[13]



NAFLD is on target to quickly becoming the main indication for liver transplants in the country, with the number of healthy livers available for transplants likely to decline.[14] Children as young as five are also developing fatty liver disease through over-consumption of sugars, sodas, fructose and corn syrup and lack of exercise.[15] Liver transplant procedures are estimated to have an average cost of $577,100,[16] putting a tremendous burden on payers, especially self-funded employers.

Both obesity and NAFLD are often the result of poor eating habits and a sedentary lifestyle. In some cases, the fat in the liver cells builds up to the point where the liver cells swell and eventually cause inflammation. But there are usually no symptoms at this point.

In some patients, persistent inflammation causes scar tissue to form in the liver, which is also known as "fibrosis." As the inflammation continues, over time it leads to non-alcoholic steatohepatitis (NASH). The overall NASH prevalence in the adult population of developed countries has been estimated as high as 12 percent.[17]

A challenging, high-volume and chronic condition that lacks a standardized care delivery model, NASH has created a global treatment market projected to reach $21.5 billion by 2025,[18] with NASH being the leading cause of liver transplantation in the United States in the coming years.

Treatment

Lifestyle modification, including diet and exercise followed simultaneously, have been shown to reverse NAFLD and NASH, and in some cases, reverse the development of fibrosis.[19] For example, a weight reduction of 3% can reverse liver fat in 35% of patients and a reduction of 10% or more can regress fibrosis in nearly half of patients studied.

Data suggest mild to moderate activity, such as walking, can reduce liver fat, irrespective of diet. Various regimens of aerobic and resistance training have been shown to reduce hepatic fat content through improvements in insulin resistance, liver fatty acid metabolism, liver mitochondrial function and activation of inflammatory cascades. These data provide justification for the current guidelines that recommend an exercise regimen that fits with the patient's individual abilities and preferences, in order to facilitate long-term compliance with a more active lifestyle.[20]

Identifying Asymptomatic Patients

An interim look at an ongoing study of 10,000 patients with no history of liver disease found that only 44 percent of patients evaluated had what is considered normal livers based on an assessment using an innovative, non-invasive tool called FibroScan®.[21] The majority had some form of liver abnormality, ranging from elevated liver fat to liver fibrosis, including 13 percent suspected of having undiagnosed liver fibrosis or cirrhosis. Significantly, the vast majority of patients had no symptoms.

This underscores the importance of identifying asymptomatic patients who may be at risk for advancing disease for earlier intervention, while the increasing prevalence of disease shows the importance of regular assessment.

Echosens' FibroScan®

This innovative tool used in the above study, FibroScan®, is a rapid, non-invasive and painless exam that offers quick insight into liver health to quantitatively estimate liver fat content and liver stiffness. It provides biomarkers that can be used not only to diagnose, but also monitor liver health, providing immediate results for the treating clinician.

As part of its collaboration with Echosens, NASHNET, a global Centers of Excellence Network represented by leading healthcare systems committed to NASH care delivery innovation, will collect and analyze data on 6,500 patients over a one-year period to identify cost effective patient flows to screen, diagnose and manage patients with NAFLD and NASH.

To accomplish this goal, the NASHNET steering committee is recommending that FibroScan® devices be placed within their primary care and/or diabetic clinics. With a goal to create an optimal care delivery model, NASHNET will also utilize FibroScan® and associated screening tests in primary care, endocrinology and bariatric clinics.

Furthermore, FibroScan® is the most widely studied tool for quantitative liver assessment in point of care in the world, with over 2,500 peer-reviewed research publications. Over 1,200 FibroScan® systems have been placed in the United States, with the expectation that FibroScan® could eventually become an important component of point-of-care protocols in the doctor's office or other healthcare setting, performed as a routine part of patient management.

Supporting the Primary Care Setting

Highly sensitive and non-invasive, FibroScan® risk-stratifies patients suspected of having liver disease, saving practice and health plan expenses of utilizing a technician to perform an ultrasound and eliminating the need for a radiologist/specialist to interpret results or recommend expensive follow-up testing for patients.

In primary care, risk-stratification is critical for identifying patients with progressive liver disease, elevated cancer risk and elevated cardiovascular risk. It also improves patient outcomes by helping to identify asymptomatic liver disease before it becomes symptomatic, provides quantitative output -- which can be used to create scores to simplify risk stratification -- and delivers consistent quantitative results. Moreover, FibroScan® is the only tool readily available and affordable to monitor fatty liver disease, especially giving feedback to patients regarding their efforts with diet and exercise.

Collectively, these factors can potentially reduce referral cost/risks of over- and under-referral and allows for earlier, targeted interventions. In the future, when combined with blood biomarkers, FibroScan®-based scores may be a cost-effective approach for monitoring patients on treatment or before treatment in the primary care setting.

The FAST score, for example, is a tool that combines the quantitative measurements of VCTE™ and CAP™ from the FibroScan® examination with AST, a commonly measured circulating biomarker to measure inflammation, to identify the probability of active fibrotic-NASH among patients who are suspected of having NAFLD.[22]

FibroScan® is designed to provide consistent measurements of liver fat and liver stiffness, allowing clinicians and researchers to advance their understanding of the progression of liver diseases and inform patient management strategies. What's more, the output supports the use of standardized scoring algorithms for longitudinal monitoring of liver health and for populating patient care plans by generalists in real-time. These scores simplify the diagnostic and patient management strategies at the generalist practitioner level.

Risk stratification with FibroScan® at point of care can reduce overall diagnosis costs by better identifying patients needing a more comprehensive specialist workup, as well as avoiding unnecessary costly procedures or diagnostic workups for others. FibroScan® also enhances patient satisfaction with health plan membership and improves member recruitment for Medicare Advantage and Medicaid Managed Care.

Reversing Liver Damage and Diabetes

Dr. Russell Yang, M.D., Ph.D., FACP, FASGE, and Dr. Jodi Nishida, Pharm.D., at Hawaii Gastro Health and The Keto Prescription, have found that rapid weight loss is key in reversing liver damage and diabetes. It is well documented that reducing calorie intake with the Mediterranean diet, keto diet, DASH diet, bariatric surgery or medications can have a positive effect.[23]

One effective strategy is the ketogenic diet, which emphasizes a low carbohydrate plan, with moderate protein and high levels of healthy fats, such as virgin olive oil, avocados and cheese. In fact, they have been able to document a complete reversal of Stage Three steatosis (fatty liver change) in less than two months.

The FibroScan® score is also used in their practice to demonstrate the impact of the weight loss via the ketogenic diet and the benefits of being in a state of ketosis -- a metabolic state in which fat provides most of the fuel for the body. Patients respond well to monitoring their improvements.

Source[24]

Effective Collaboration for Chronic Care Disease Management

Given the challenge of low compliance in lifestyle changes, MetaPhy Health's Comprehensive Chronic Disease Management (CCDM) program including Chronic Care Management and Remote Patient Monitoring can make weight management more effective in treating fatty liver and its underlying conditions. A CCDM program focused on lifestyle management will achieve a long-term impact and prompt rapid and potentially meaningful changes in liver fat as estimated by CAP ™, which will further validate the program's lifestyle interventions.

It is estimated that of the 16.5 million Americans with fibrotic-NASH, approximately 1.5 million are currently under the care of gastroenterologists. Of these, approximately .5 million are potential candidates for drug treatment, while another .7 million have earlier stage fibrotic disease and, while they have progressive disease, they are not yet candidates for treatment. For gastroenterology and hepatology-gastroenterology practices, partnering with MetaPhy can improve efficiency around lifestyle modifications and tailored programs for each patient—with the hope of arresting or even reversing advancing liver disease.

FibroScan® is a powerful tool supporting outcomes and providing valuable information on liver health. This information can support care management across key components of the metabolic syndrome – diabetes and hyperlipidemia.

As part of a patient-centered care model, FibroScan® is designed to improve individual health outcomes, lower payer costs by avoiding expensive, invasive interventions and enhance the financial performance of practices.

As an ancillary program, an effective and efficient CCDM program can mitigate the impact of NAFLD on metabolic comorbidities. With the introduction of new treatment options, including drugs that will soon be available, a targeted CCDM program can integrate non-invasive, point of care liver examinations to leverage the launch of these drugs in a way that improves outcomes, lowers costs and enhances the physician practice income stream.

Real World Example

Dr. Reed Hogan, M.D., GI Associates (GIA) in Flowood, Mississippi, has successfully integrated its FibroScan® capabilities with the MetaPhy CCDM programs. With this partnership, GIA is able to provide services to patients across the spectrum of NAFLD, leveraging FibroScan® to monitor and engage patients. Effective lifestyle modification has been shown to cease and often reverse the progression of fibrotic NASH.

GIA is not only experiencing fiscal benefits from its NAFLD program, but also providing a valuable service to its community where viable treatment options for NAFLD have traditionally been scarce. In the GI setting where the volume of NAFLD/metabolic syndrome patients is overwhelming, the profitability of CCDM drives this ancillary.

Supporting Payer Goals

As a reliable tool in the front-line battle against a liver disease epidemic, and in the absence of drugs made specifically to treat NAFLD, FibroScan® aligns with payer goals of enhancing care quality in a way that reduces costs and improves outcomes.

Furthermore, FibroScan® improves access to care, provides sensitive testing at point of care to reduce unnecessary specialist referrals and allow for earlier, targeted interventions. It also enables consistent tracking of liver health over time and rules out those who don't need more testing while focusing resources on those who do. For example, patients with Type 2 diabetes may be at a higher risk for progressive liver disease. FibroScan® also establishes liver health in the chronic care management of patients with metabolic syndrome.

This innovative tool can also enhance population health management by improving diagnosis accuracy at the point of care to allow for better accounting for health risks among the populations served and negotiating rates with employers.

Future Hopes of Reversing Liver Disease

For now, the best way to reverse liver damage is through weight loss, whether through lifestyle changes or weight-loss surgery. In one study, researchers found that individuals who achieved a weight loss of 10% or more after one year of lifestyle changes involving a low-calorie diet and exercise experienced reductions in NAFLD. In addition, 90% of people with a >10% weight loss experienced resolution of NASH, and 45% showed regression of fibrosis, the formation of fibrous scar tissue. Weight loss of 7-10% also reduced disease severity in some patients, including men and those without diabetes.

Promising drugs are also emerging to help reverse liver damage. Novo Nordisk's popular GLP-1 diabetes drug semaglutide—a weight loss drug—has also generated encouraging clinical results. Further studies are needed to see if semaglutide can reverse fibrotic-NASH. Novo states that its clinical results represent "the largest NASH resolution improvement so far," confirming that the drug could be a potent anti-NASH agent.

Also in the pipeline, obeticholic acid (OCA), has shown it can improve liver fibrosis in 23.1% of patients, almost double the 11.9% rate investigators observed with placebo. OCA could be the first drug approved to treat fibrotic-NASH.

With the introduction of new treatment options, a targeted CCDM program can help cost-effectively assess and manage the risk factors for NAFLD. Consistent scoring of liver stiffness and fat with FibroScan® is likely to play an increasingly important role in supporting the launch of these drugs in a way that improves outcomes and lowers costs for employers and payers.

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About Echosens

Echosens, the developer of FibroScan®, is an innovative high-technology company offering a full range of products and services supporting physicians in their assessment and management of patients with chronic liver diseases. FibroScan is supported by over 2,500 peer-reviewed publications and examinations are covered by Medicare, Medicaid and many insurance plans. For more information, please visit http://www.echosens.us and follow us on Twitter (@echosensNA).

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