

# Overscreening Leads to Overdiagnosis of MASLD

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**M**etabolic dysfunction–associated steatotic liver disease (MASLD), formerly nonalcoholic fatty liver disease, is a chronic condition characterized by fat accumulation in the liver and associated with other metabolic abnormalities.<sup>1</sup> The change in nomenclature reflects that diagnosis requires at least one metabolic abnormality (eg, obesity, type 2 diabetes, hyperlipidemia, hypertension), not the lack of alcohol consumption alone.<sup>1-3</sup> Prevalence of MASLD in the United States is approximately 1 in 4 adults.<sup>2,4</sup>

A clinical review article in this issue of *American Family Physician (AFP)* defines MASLD and outlines its diagnosis and treatment.<sup>5</sup> In a 2022 *AFP* article, we recommended against screening for MASLD because it is unlikely to improve prognosis and could lead to overdiagnosis and overtreatment due to low hepatic mortality, high false-positive rates, and limited pharmacologic treatment options.<sup>6</sup> Overdiagnosis, the diagnosis of conditions that would never cause symptoms or harm, results in unnecessary labeling of patients with disease.<sup>7,8</sup> It harms patients by prompting overtreatment, often leading to psychological complications (eg, anxiety, depression) associated with disease labeling and increased financial burden from medical expenses and time away from work.<sup>8,9</sup> Physical harm may occur, including complications from unnecessary testing, diagnostic procedures, and treatment with expensive, unproven medications.<sup>8-10</sup> Clinical recommendations based on broadened disease definitions often lead to use of nonbeneficial screening tests and treatment modalities, as demonstrated by MASLD.<sup>7,8</sup>

Population-based universal screening for MASLD is not recommended because evidence of benefit is lacking.<sup>2,11</sup> Less than 10% of patients with MASLD progress to severe fibrosis or cirrhosis with increased risk of developing hepatocellular carcinoma.<sup>1-3</sup> Cardiovascular disease and extrahepatic cancers are the primary causes of mortality in patients with MASLD, with liver-associated complications causing less than 10% of deaths.<sup>1-3</sup> Most hepatology societies recommend a sequential,

risk-stratified approach to identifying patients with MASLD.<sup>1,11</sup> However, the American Diabetes Association 2026 Standards of Care recommends that adults with prediabetes or type 2 diabetes be screened for fibrosis, including those with normal liver enzymes, using a calculated Fibrosis-4 index, with elastography for those who have indeterminate or abnormal Fibrosis-4 scores.<sup>12</sup> In the United States, approximately 98 million adults (more than 1 in 3) have prediabetes, and approximately 38.4 million (11.6%) have diabetes, meaning the American Diabetes Association advocates for screening nearly half the adult population for MASLD.<sup>12,13</sup> Elastography is a noninvasive alternative to liver biopsy for assessing liver fibrosis.<sup>14</sup> Its use in patients who are obese is limited and often leads to use of magnetic resonance elastography and potentially harmful liver biopsy.<sup>7,14</sup>

Lifestyle modifications (eg, dietary changes, physical exercise, smoking cessation, alcohol cessation) and treatment of underlying causes are essential to prevent hepatic steatosis and reduce most metabolic and cardiovascular risk factors.<sup>11,15</sup> Semaglutide (Ozempic, Wegovy) and resmetirom (Rezdiffra) are approved by the US Food and Drug Administration for treatment of MASLD. Semaglutide, other glucagon-like peptide-1 (GLP-1) receptor agonists, and dual glucose-dependent insulinotropic polypeptide with GLP-1 receptor agonists are indicated to treat comorbidities related to MASLD, making diagnosis of MASLD unessential. Resmetirom, an oral, liver-directed thyroid hormone receptor beta agonist, has shown histologic benefit in patients with moderate (F2) to severe (F3) fibrosis. The average wholesale price of this medication is \$57,670 annually, although a cost-effectiveness analysis suggests it does not meet value-based treatment thresholds.<sup>16</sup> With minimal efficacy, high cost, and no long-term data on patient-oriented outcomes, use of resmetirom should be reserved for patients with severe fibrosis.<sup>1,2,11</sup>

Although 25% to 30% of patients with MASLD and metabolic dysfunction–associated steatohepatitis develop advanced fibrosis within 8 to 10 years of diagnosis, adding another chronic disease label does not necessarily improve their prognosis or address the underlying cause of their poor health status, especially if comorbidities are already being treated.<sup>15</sup> Many factors promote overdiagnosis, including growing use of advanced diagnostic testing, poor financial incentives, and a medical culture that encourages greater use of tests

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and treatments.<sup>7-9</sup> Lifestyle modifications and treatment of underlying conditions, without disease labeling that causes emotional, clinical, and financial burdens, are appropriate to prevent and treat MASLD. Overdefinition through broadened diagnostic criteria often leads to more harm than benefit.<sup>8,9</sup> Family physicians need to restore a health care system that focuses on person-centered care, emphasizing appropriate screening, wellness, and health, instead of sick care and disease-oriented diagnoses, diagnostic procedures, and therapeutics that often prioritize profit over patients.

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