Making Sense of the Nonalcoholic Fatty Liver Disease Clinical Practice Guidelines: What Clinicians Need to Know

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Standards of care summarized in clinical practice guidelines for nonalcoholic fatty liver disease (NAFLD) offer clinicians a streamlined diagnostic and management approach based on the best available evidence. These recommendations have changed a great deal in recent years; today, there is a clear focus on screening for the early identification and risk stratification of patients at high risk of steatohepatitis and clinically significant fibrosis to promote timely referrals to specialty care when needed. This article reviews and provides the rationale for current guidelines for NAFLD screening, diagnosis, treatment, and monitoring and addresses barriers to providing evidence-based NAFLD care and how to overcome them. The current paradigm of care calls for primary care clinicians and specialists to work together, within a multidisciplinary care team familiar with obesity and diabetes care, to provide comprehensive management of these complex patients.

The impact of nonalcoholic fatty liver disease (NAFLD) in people with type 2 diabetes is just now beginning to be fully appreciated. This understanding has been driven, at least in part, by recent alarming studies about the magnitude of the problem in individuals with type 2 diabetes, as elegantly reviewed in depth elsewhere in this article collection (1). In the United States, >70% of people with type 2 diabetes have hepatic steatosis, and many have nonalcoholic steatohepatitis (NASH), the more severe form with inflammation, hepatocyte necrosis, and significant fibrosis (2–5). Having NASH carries a significant risk of future cirrhosis, especially in the presence of obesity and type 2 diabetes (6,7), and even of hepatocellular carcinoma (HCC) (8), and increases the risk of developing type 2 diabetes and cardiovascular disease (CVD) (9–11). Patients with type 1 diabetes, particularly those with obesity, are also at risk for cirrhosis from NASH (12). Cirrhosis from NASH will soon be the most common cause of liver transplantation in the United States (13).

Against this backdrop, many patients and clinicians are unaware of the health risks posed by NAFLD and the condition often remains untreated (14–16). However, some medications approved to treat obesity or type 2 diabetes—namely, pioglitazone and glucagon-like peptide 1 (GLP-1) receptor agonists—can reverse steatohepatitis and are recommended by all recent clinical practice guidelines (12,13,16,17); yet, these medications are not widely prescribed. Proper management of comorbidities could greatly reduce CVD and all-cause deaths in people with NAFLD (18). Table 1 puts into perspective our current situation with NAFLD and how it compared with just a few decades ago with regard to microvascular diabetes-related eye or kidney disease and osteoporosis, before routine early screening for those conditions was broadly adopted.

This review walks readers through the recent evolution of and rationale for current NAFLD guidelines for fibrosis risk stratification in people with diabetes, with special emphasis on the NAFLD recommendations in the American Diabetes Association's (ADA's) *Standards of Care in Diabetes—2023* (17). All current guidelines agree on the same stepwise diagnostic and management process for individuals at high risk for NASH and cirrhosis. We also discuss the current and future impact of NASH on primary care, the barriers and opportunities that can arise in caring for these complex patients, and some recommended strategies (e.g., embedding guidelines into our electronic health record [EHR] systems to rapidly risk-stratify high-risk patients for future cirrhosis) to improve implementation of the recommended clinical care algorithm.

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TABLE 1 Examples of Screening and Intervention Strategies That, as for NAFLD, Can Improve Quality of Life and Reduce Complications in People at High Risk

Feature	Nephropathy and Retinopathy in Diabetes (Since the 1970s)	Osteoporotic Fractures (Since the 1990s)	NASH (Since the 2000s)
Long natural history	Yes	Yes	Yes
High prevalence	Yes	Yes	Yes
Major cause of morbidity	Yes	Yes	Cirrhosis, HCC, CVD
Increased mortality	Yes	Yes	Yes
Screening tests	Microalbuminuria in chronic kidney disease; dilated eye exams for retinopathy	Bone mineral density	First line: FIB-4 index; second line: transient elastography* and other diagnostic blood tests†
Adequate treatments	Not initially, but approved agents are available today	Not initially, but approved agents are available today	Not yet, but some diabetes medications with efficacy in NASH are available today

*Vibration controlled transient elastography (VCTE) allows for estimation of liver stiffness measurement (LSM), a validated surrogate of hepatic fibrosis. †Enhanced liver fibrosis (ELF) is the preferred second-line blood test (12,13,17); other tests (e.g., PRO-C3 [N-terminal propeptide of type III collagen] and NIS4/NIS2+ [blood-based biomarker panels]) are under development.

Evolution of Clinical Care Pathways

The term "nonalcoholic steatohepatitis" was coined by Ludwig et al. (19) in 1980. They described 20 cases of individuals with steatohepatitis that histologically mimicked alcoholic hepatitis (i.e., with steatosis, lobular inflammation, focal necrosis, and often fibrosis), of whom three had cirrhosis. Most of these individuals had obesity and many had diabetes. The twin epidemics of obesity and type 2 diabetes have greatly accelerated since then, triggering an epidemic of NAFLD and cirrhosis from NASH (20). However, as recently summarized (21), until about 2020, recommendations for screening and risk stratification were not consistent across medical professional organizations and focused mainly on case-finding of steatosis by ultrasound and/or elevated plasma aminotransferase levels >40 units/L, with the possible use of noninvasive tests such as the Fibrosis-4 (FIB-4) index, the NAFLD fibrosis score, or the APRI [AST-to-platelet ratio index]). They did not, however, recommend systematic screening for patients at high risk of liver fibrosis, such as those with type 2 diabetes.

Table 2 summarizes the evolution in U.S. clinical practice guidelines since 2020. In an effort endorsed by the ADA and other medical associations, the American Gastroenterological Association (AGA) in 2021 gathered a multidisciplinary group of gastroenterologists/hepatologists, endocrinologists, and primary care professionals (PCPs) to write a call to action that detailed the magnitude of the epidemic and the need to screen high-risk individuals and aggressively treat disease drivers such as obesity and type 2 diabetes based on NASH fibrosis stage (21). This white paper was published simultaneously in the official journals of the ADA (*Diabetes Care*) (21), AGA (*Gastroenterology*) (22), and The Obesity Society (*Obesity*) (23), as well as in the journal *Metabolism* (24). In 2022, the American Association of Clinical Endocrinologists (AACE), in an initiative cosponsored by the American Association for the Study of Liver Disease (AASLD), expanded

TABLE 2 Evolution of Recent NAFLD Clinical Practice Guidelines

- **Recommendations up to 2020**
  - ✓ Screening and risk stratification not consistent across published guidelines
- **American Gastroenterological Association 2021 (endorsed by the American Diabetes Association) (16,21–24)**
  - ✓ White paper: call to action by experts from hepatology, endocrinology, primary care, and obesity management for case-finding, referral, and management
  - ✓ Multidisciplinary clinical care pathway
- **American Association of Clinical Endocrinologists 2022 (cosponsored by the American Association for the Study of Liver Disease) (12)**
  - ✓ The first in-depth diagnostic and management approach to NAFLD for PCPs and endocrinologists
- **American Association for the Study of Liver Disease 2023 (13)**
  - ✓ Update of the 2018 AASLD recommendations: aligns with AGA 2021 and AACE 2022 guidelines
- **American Diabetes Association 2023 (17)**
  - ✓ Updated NAFLD recommendations in the *Standards of Care in Diabetes—2023:* offer new guidelines for cirrhosis risk stratification and the management of people with prediabetes or type 2 diabetes

on the magnitude of the problem and provided a detailed rationale for screening and treating people at high risk of significant fibrosis (stage ≥F2), including those with prediabetes (particularly with obesity) or type 2 diabetes, those with obesity and two or more cardiometabolic risk factors, and anyone found incidentally to have steatosis or elevated plasma aminotransferase levels ≥30 units/L (12).

In 2019, the ADA recognized for the first time the health care threat posed by NAFLD/NASH in its *Standards of Medical Care in Diabetes—2019* (25), and, in 2021, it endorsed the AGA recommendations and incorporated them into its Standards of Care that year (26). These initial recommendations have been greatly expanded in the 2023 Standards of Care (17) to include 14 specific recommendations (discussed further below). In 2023, AASLD also updated its 2018 recommendations to support universal FIB-4 index screening of all people with prediabetes or type 2 diabetes (13).

Finally, as discussed elsewhere in this article collection (1), experts in this area have recently proposed replacing the term "nonalcoholic fatty liver disease" with "metabolic dysfunction–associated steatotic liver disease" (MASLD) (27,28) and to update the definition to include, in addition to steatosis, at least one cardiometabolic risk factor associated with insulin resistance. A new category known as "MetALD" has been used to refer to individuals with alcohol intake greater than in NAFLD but less than in alcoholic liver disease. These changes aim to remove potential patient stigma (e.g., the use of "fatty" for steatosis) and to include cardiometabolic risk factors as surrogates for insulin resistance and metabolic dysfunction.

The new definition does not affect people with prediabetes or type 2 diabetes, who by virtue of their diagnosis are already considered to have a cardiometabolic risk factor. Because ~75% of people in the United States have overweight or obesity and 85% have one cardiometabolic risk factor even without steatosis (29), the new definition overall appears to correlate well with NAFLD.

Its limitations include the need for better validation of the specificity of different cardiometabolic risk factors as surrogates for insulin resistance (e.g., specificity may be low for hypertension and much higher for type 2 diabetes, making the reliance on just one cardiometabolic risk factor a potentially unreliable marker for insulin resistance in some patients). Cardiometabolic risk factors are often caused by multiple, poorly understood pathways beyond insulin resistance, and applying risk factors that were identified to predict cardiovascular risk and type 2 diabetes (30) to the diagnosis of liver disease runs the risk of reviving controversial issues about cutoffs and definitions of metabolic syndrome for the diagnosis of NAFLD (31). Also, not all people with diabetes have steatosis from insulin resistance (i.e., some may have insulin secretion defects and not insulin resistance, or missed secondary causes). Finally, some people may have insulin resistance and steatosis without obvious cardiometabolic risk factors, such as in younger adults often seen in PCP clinics. Thus, more work is needed to validate and add greater precision to the definition of MASLD.

Diagnostic Pathway for Groups at High Risk of Developing Cirrhosis

The ADA (17), the other U.S. clinical practice guidelines mentioned above (12,13), and similar recommendations abroad (32,33) agree on the need for FIB-4 index fibrosis screening of high-risk individuals. People with type 2 diabetes have the greatest risk, which is worsened by overweight or obesity. Figure 1 summarizes the ADA's 2023 screening strategy, which is based on initial screening/fibrosis risk stratification with the FIB-4 index, which is calculated from age, ALT, AST, and platelet count. A FIB-4 index calculator is available online (www.mdcalc.com/calc/2200/fibrosis-4-fib-4-index-liver-fibrosis). This strategy is a departure from the older paradigm of screening only if plasma aminotransferase levels are >40 units/L because many individuals with diabetes and NASH who have clinically significant fibrosis (stage ≥F2) have plasma aminotransferase levels <40 units/L (2,3,34,35). Normal ALT cutoffs are 29–33 units/L for males and 19–25 units/L for females because higher levels are associated with increased liver-related mortality (36).

The FIB-4 index was chosen for its low cost, simplicity, and reasonable specificity, although its sensitivity is far from ideal. Most individuals with an index value <1.3 will have a low, or lower, risk of having advanced fibrosis (stage F3–F4) or negative liver outcomes (Figure 1). A higher value, especially if >2.67, indicates a high, or higher, probability of advanced fibrosis (state F3–F4) and adverse liver outcomes (17,37). A value >1.3 is the cutoff calling for a second test, as discussed below. Moreover, the FIB-4 index predicts future major adverse cardiovascular events, hospitalization for heart failure, and cardiovascular death (38). Therefore, this tool can help clinicians monitor changes in liver fibrosis and predict hepatic decompensation and other complications, as well as liver-related mortality (39,40). Of note, given the impact of age in the FIB-4 index calculation, this tool should not be used in people <35 years of age and should be used with caution in those ≥65 years of age, in whom higher cutoffs should be considered (17).

The aim of risk stratification is to find clinically significant liver fibrosis, defined as ranging from moderate (stage F2)

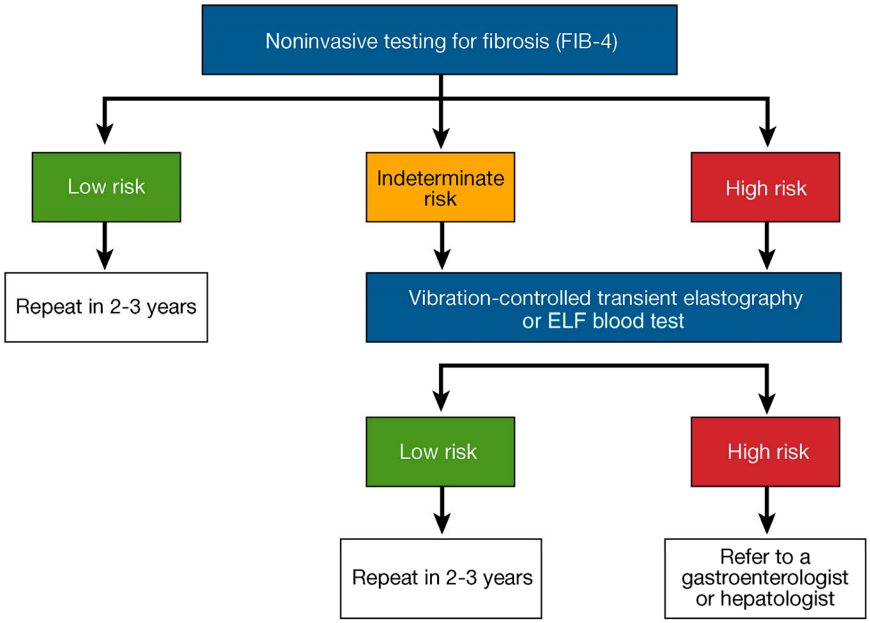

FIGURE 1 Algorithm for risk stratification of individuals with NAFLD or NASH. Reprinted with permission from ref. 17.

to cirrhosis (stage F4) from NAFLD, even if they have normal liver enzymes. At stages ≥F2, there is a greater risk of cirrhosis, HCC, and all-cause mortality (41). Extrahepatic cancer (13), progression from prediabetes to type 2 diabetes (7), and CVD (9) also increase significantly at stages ≥F2. People with type 1 diabetes are also at risk (42,43), especially in the presence of obesity, a condition that affects about one-third of this population in the United States. Therefore, AACE (12) and ADA (17) recommend screening for people with type 1 diabetes only if additional risk factors for NAFLD, such as obesity, steatosis, or elevated ALT, are present. Clinicians must remember to always consider secondary causes of liver disease other than NAFLD, especially when there are persistently elevated plasma aminotransferase levels for >6 months.

When the FIB-4 index value is >1.3 (the low risk cutoff), a second-line test is recommended such as a liver stiffness measurement (LSM) using transient elastography, if available, or an enhanced liver fibrosis (ELF) test (Figure 1) (17). Transient elastography and the ELF test predict future morbidity and mortality in NAFLD, as reviewed elsewhere (12,13). The LSM cutoff of <8.0 kPa indicates no need for referral to a gastroenterologist/hepatologist because it suggests a low risk for clinically significant fibrosis (stage ≥F2) (44,45). When to repeat LSM surveillance testing in someone with a FIB-4 index value >1.3 is uncertain at present, but the current recommendation is to repeat the test every ≥2 years (17). However, if LSM is >12 kPa, the risk for advanced fibrosis is high, whereas an LSM ≥8 kPa and <12 kPa is indeterminate for advanced fibrosis (or intermediate risk). The ADA strongly recommends that people with diabetes who are at indeterminate (LSM ≥8 kPa but <12 kPa) or high (LSM >12 kPa) risk of fibrosis be referred to a hepatologist or gastroenterologist for further evaluation based on each practice's referral setting (46–48). MRI techniques, when indicated, can quantify liver fat (proton magnetic resonance spectroscopy or MRI-proton density fat fraction) or necroinflammation with risk of fibrosis (LiverMultiScan cT1) or further assess liver stiffness by elastography (MRI and elastography) (13). However, the high cost and limited availability of MRI techniques make them more cost-effective when used by liver specialists. Liver biopsy remains the gold standard for the diagnosis of NASH but is usually indicated at the discretion of a specialist (13,17).

Impact of NAFLD on the Management of Type 2 Diabetes and Cardiometabolic Risk Factors

The task at hand for clinicians may appear at first overwhelming. With 37.3 million people in the United States currently having type 2 diabetes and NAFLD affecting >70% of them, this means there are at least 26 million people with type 2 diabetes and NAFLD at risk for cirrhosis. This estimate does not account for people with type 1 diabetes and obesity, who are also at risk. Based on recent findings of a prevalence of cirrhosis in NASH of 3–5%, >1 million people with diabetes in the United States may have undiagnosed cirrhosis. Overall, the management of type 2 diabetes today is well standardized in terms of glycemic control,

weight management, and cardiovascular risk reduction (17). However, the presence of NAFLD adds layers of complexity to diabetes management, including the need for specific pharmacotherapy to treat obesity and diabetes, to improve quality of life and avert cirrhosis and CVD in these patients.

Role of Pharmacotherapy With Glucose-Lowering Medications in NASH

The pharmacological management of NAFLD is discussed in depth elsewhere in this article collection (49). In brief, there are no medications approved by the U.S. Food and Drug Administration for the treatment of NASH; however, cirrhosis prevention is possible with available glucose-lowering agents. Guidelines from the ADA (17) and other organizations (12,13) recommend treating hyperglycemia with pioglitazone or a GLP-1 receptor agonist in adults with type 2 diabetes who have biopsy-confirmed NASH or are suspected of having clinically significant liver fibrosis (stage ≥F2) assessed by noninvasive tests. Other glucose-lowering medications lack evidence of benefit in NASH.

GLP-1 receptor agonists are safe and effective in reversing steatohepatitis in proportion to the magnitude of weight loss achieved with the therapy (50). When possible, clinicians should prescribe a GLP-1 receptor agonist with proven benefit to reverse steatohepatitis from randomized controlled trials (RCTs) (e.g., liraglutide and semaglutide). The most common side effects are gastrointestinal in nature, but these agents overall are well tolerated. Tirzepatide, a dual GLP-1 and gastric inhibitory polypeptide agonist, reduces hepatic steatosis (51) and is being tested in an RCT with liver histology as the primary outcome. A number of new agents for the treatment of obesity will radically change obesity management in the future (52).

Six paired-biopsy studies have shown that pioglitazone reverses steatohepatitis in people with type 2 diabetes and treatment duration of 6 months to 3 years (53,54), as reviewed elsewhere in this article collection (49). It may cause regression, or at least slow the progression, of liver fibrosis (55). Pioglitazone may cause weight gain (mean of 1–2% with 15 mg/day and 3–5% with 45 mg/day) or lower-extremity edema (in ∼5% of people), but these effects can be avoided with the use of lower doses, nutrition counseling, or concomitant therapy with a sodium–glucose cotransporter 2 inhibitor or a GLP-1 receptor agonist (49). Pioglitazone therapy should be avoided in patients with heart failure, bladder cancer (although this contraindication is controversial), or osteoporosis.

Insulin is the preferred glucose-lowering agent in adults with diabetes and decompensated cirrhosis because data on the safety of oral agents and GLP-1 receptor agonists in this setting are limited (56); however, a short-term study suggested that semaglutide may be safe in patients with compensated cirrhosis (57).

Finally, although there is lingering controversy about the potential of vitamin E to increase risks of prostate cancer and of CVD, this treatment has proven to be beneficial for NASH in people without diabetes (58), with modest evidence to date in people with type 2 diabetes (59).

Cardiometabolic Risk of NASH in People With Coexisting Type 2 Diabetes

Adults with type 2 diabetes and NAFLD have an increased risk of CVD. A comprehensive approach to cardiovascular risk reduction includes lifestyle modification and pharmacotherapy for most patients. This population often has severe insulin resistance that has a deleterious impact on the natural history of NASH and promotes cirrhosis (20). Individuals with overweight or obesity should be encouraged to implement lifestyle changes that promote weight loss and reverse NAFLD, ideally within a structured nutrition and exercise program (17). The Mediterranean diet is the most recommended eating pattern for long-term liver and cardiometabolic health. As reviewed elsewhere in this article collection (60), improvement in steatosis begins to occur with a weight loss of ∼5%, with improvement in steatohepatitis generally requiring a 5–10% weight loss and improvement in fibrosis requiring an even greater reduction in weight.

The ADA considers the use of statins to be safe and to reduce overall mortality in people with NASH and compensated cirrhosis (17). Metabolic surgery by an experienced surgical team should be considered in appropriate people with NAFLD and type 2 diabetes—even in those with compensated cirrhosis—to improve steatohepatitis and cardiometabolic health. However, it is not recommended in those with decompensated cirrhosis because of increased risk of morbidity and mortality (12,13,17).

To summarize, early screening of cardiometabolic risk is essential for people with type 2 diabetes and NAFLD, and cardiovascular risk reduction requires a comprehensive approach, including pharmacotherapy, to adequately manage weight, glycemia, and other cardiometabolic risk factors.

Barriers to and Opportunities in the Management of NAFLD

There are several challenges to following NAFLD (21,61,62) and other (63) clinical practice guidelines in general, and, in many cases, overall adoption can be suboptimal. The

seemingly exponential growth in the general body of medical research and knowledge corresponds with equally multiplying guidelines and recommendations. As a result, one significant barrier to the adoption of NAFLD clinical practice guidelines is a lack of practitioner awareness, partially because these guidelines coexist with so many other disease recommendations (61,64,65). There are currently 104 published recommendations from the U.S. Preventative Services Task Force alone (66), 14 adult immunization recommendations from the Centers for Disease Control and Prevention (67), and individual guidelines from specialty professional organizations for many disorders. This plethora of guidelines becomes even more complicated by their frequent revisions, reflecting the constant flux and evolution in the treatment of many diseases. Clinicians facing this increasing number of clinical practice recommendations that need to be implemented in practice may find it very challenging to stay up-to-date with each set of guidelines. A casual awareness of or familiarity with NAFLD recommendations may not lead to correct application of them into practice (62,65). One positive aspect of NAFLD guidelines in particular is their consistency and relative simplicity. They all recommend as a first step use of the FIB-4 index, which is already available in many EHR systems, followed by transient elastography or an ELF test if the FIB-4 index value is >1.3 (Figure 1).

Time can also be a significant barrier in busy clinics trying to incorporate screening and management of NAFLD with other preventive care tasks, especially when these tasks seem unrelated to patients' acute problems (61,63). Clinicians may believe there is simply not enough time available to educate patients about NAFLD and screen them when multiple health concerns must be handled during each visit.

Clinical inertia and lack of motivation to change practice habits may further hinder adoption of the guidelines by clinicians and patients alike (21,61,62,68,69). Additionally, some clinicians have an erroneous perception that NAFLD happens infrequently in their patients because it is usually asymptomatic or that it will rarely lead to cirrhosis, and, it is not worth investing time and effort to perform screening and risk stratification.

A lack of resources, such as limited availability of elastography and high costs of proprietary biomarker testing and MRI studies, can also be restrictive. These system barriers may be overcome with appropriate institutional leadership, the development of a multidisciplinary care team, and recurrent professional education about clinical practice guidelines for all health care professionals involved in screening and managing patients (48). Such efforts are actively underway across the United States (21) and globally (70,71) and are radically changing models of care for NAFLD (47).

Despite these barriers, there are many opportunities to improve universal uptake of NAFLD guidelines. Continuing education opportunities for clinicians, with an emphasis on the significant potential morbidity and mortality of NAFLD and the benefits of guideline-recommended screening and management, will increase awareness and reduce inertia. Further refining current clinical pathways (CPWs) and making use of automated tools within EHR systems may also ease limitations related to time constraints, lack of awareness, the challenges of real-time implementation in clinical practice, and the need to keep up with frequent guideline revisions and updates.

New Tools for NAFLD Management Moving Forward

The translation of NAFLD guidelines into a concise and practical algorithm in the form of a CPW, which can be incorporated easily into EHR systems, has already helped and will likely bridge the gap from evidence to practice in the near future (72,73). The aims of the CPW is to seamlessly harmonize NAFLD guidelines with clinical workflow as a roadmap to acquire condensed, high-yield information to guide care delivery, to reduce variation among health care settings, and to improve quality of care, and, ultimately, health outcomes. Further coupling the CPW with EHR-based tools has the advantages of more widely disseminating the CPW and updates at an institutional level and providing support in patient-specific assessments and clinical decision making. EHR-based tools have been shown to improve compliance with NAFLD (48) and many other practice guidelines (74–76) and can be applied specifically to the screening, risk stratification, and management of NAFLD at the point of care.

EHR-integrated CPWs (E-CPWs) can enhance screening of NAFLD and prompt for entry into the pathway based on rapid review of risk factors and demographics. After clinicians approve entry into the E-CPW, reminders for appropriate studies to be ordered and decisions can be tracked effectively over time. For example, an E-CPW can prompt for and prepare order sets for laboratory tests to calculate the FIB-4 index value for a clinician's approval. The E-CPW can automatically calculate the FIB-4 index value, provide the result, assist with interpretation, and suggest next steps in the CPW based on current guidelines. Such integration of work in this field is happening at the University of Florida (Gainesville, FL) and at many academic institutions in the

United States (K.C., J.B., personal communication). Similarly, an E-CPW can prepare elastography orders for approval when indicated, automatically pull in the LSM, and guide patient management based on the result. Clinicians in primary care, endocrinology, and hepatology can collaborate and share the use of an E-CPW to stay informed about the NAFLD status of patients they are comanaging. Such efforts are likely to change care in the future and improve outcomes across the spectrum of NAFLD management (77).

Role of PCPs in NAFLD Prevention and Management

It should be emphasized that most people with NAFLD receive care only from their PCP. Given that NAFLD typically has no symptoms until advanced stages of the disease (i.e., cirrhosis) and that it is associated with severe hepatic and extrahepatic morbidity and mortality, PCPs and all health care professionals involved in the care of people with diabetes will need to excel at identifying people at risk early in the disease (46). This statement should sound familiar to PCPs and endocrinologists, who likely are already identifying people with prediabetes or type 2 diabetes early, when complications can be prevented.

However, the U.S. health care system typically focuses attention on patients' primary complaints rather than on preventive care. Because the United States is an aging, sedentary, and obesogenic society, U.S. adults increasingly will develop multiple chronic conditions. This fact makes primary care visits more complex, as PCPs must balance the expectation that they will address patients' presenting complaints in addition to screening for and managing multiple chronic conditions such as NAFLD, which often have no symptoms.

How do we overcome this dilemma? Figure 2 depicts an ideal multidisciplinary team for the long-term care of people with NAFLD, with the patient and family at the center. Optimally, we should embrace a team-based care approach that includes multiple care team members working within their skill set to help patients through multiple touch points improve self-management and make lifestyle and behavior changes. This effort will require education campaigns that help patients and clinicians understand the need to see multiple care team members and how they will benefit directly from screenings and early preventive intervention. Models of care will vary across institutions (47), and many care team members can help manage patients with NAFLD (77).

Most patients with NAFLD will also have type 2 diabetes or metabolic dysfunction and may need medications such as a

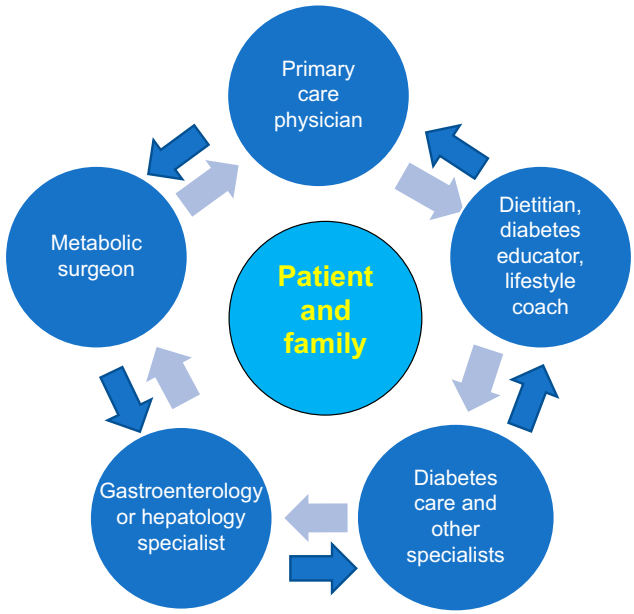

FIGURE 2 An ideal multidisciplinary team for the long-term care of people with NAFLD, with the patient and family at the center.

GLP-1 receptor agonist, which may prove difficult because of insurance coverage limitations in the primary care setting. Partnering with the endocrinologist can improve patient access to resources for managing their diabetes, including medications that could be equally beneficial for NASH (i.e., pioglitazone and, especially, costly GLP-1 receptor agonists). Furthermore, screening tools such as the FIB-4 index, the ELF test, and transient elastography allow clinicians to triage patients who would benefit from seeing a hepatologist. Using these tools will allow the medical team to refer the right patients for liver-specific care and thereby reduce liver-associated complications.

Figure 2 emphasizes the role of the team and the dynamics at play when patients seek care from multiple specialists, with visits focused on NAFLD and the comorbidities affecting it. Most importantly, any referral to specialists requires two-way communication to share expectations of the consultation and communicate back to understand how treatment plans may have been adjusted to optimize patient care. Including other team members in patient care in a multidisciplinary approach allows PCPs to focus more on therapeutic lifestyle modification such as changes in dietary habits and physical activity and to assess and address other barriers, including social determinants of health. Each member of the team brings a specific expertise and can spend more time on issues related to that expertise, complementing the approach of the PCP. Some team members may also see patients outside of the normal health care

setting, which allows for greater insight into patients' daily life and the involvement of family members.

To summarize, the implementation of established NAFLD standards of care streamlines screening and fibrosis risk stratification, which can be done simply or even automated within EHR systems. Screening and risk stratification will help to optimize resources and decrease management burden and should lead to improved patient satisfaction and quality of life, as well as health outcomes. Standards for comparing the effectiveness of different models of care should be clearly defined, both to assess results internally within health systems and for reporting in the literature (78).

Conclusion

The latest clinical practice guidelines offer streamlined diagnostic and treatment algorithms based on the best available evidence on NAFLD care. Treatment should focus on lifestyle modification to promote weight loss, if needed, and increased exercise, which may help with sarcopenia, as is common in individuals with advanced fibrosis and cirrhosis. Management should also include pharmacological treatment of obesity and/or diabetes with a GLP-1 receptor agonist or pioglitazone to reverse NASH. Close monitoring can be done with a combination of noninvasive blood tests (e.g., the FIB-4 index and the ELF test), as well as imaging (e.g., transient elastography and MRI), and rarely requires a liver biopsy.

Practical barriers to optimal care exist, including competing comorbidities and clinic visit time constraints, but these may be at least partially overcome with improved management tools. One attractive aid for busy practitioners will be the use of EHR systems with built-in FIB-4 index calculators and an E-CPW that can assist them, saving time and helping to navigate management of the disease from screening, to treatment and ongoing monitoring.

NAFLD calls for PCPs to work collaboratively with endocrinologists/diabetologists, advanced practice providers, health care professionals involved in obesity management and diabetes care (e.g., nutritionists, behavioral modification specialists, and surgeons), gastroenterologists/hepatologists, and other specialists to ensure a comprehensive approach to these complex patients. It is now in our hands to use the ADA's recommendations and other guidelines wisely to prevent cirrhosis (even HCC) and CVD in our patients with NAFLD.

DUALITY OF INTEREST

K.C. has received research support toward the University of Florida as a principal investigator from Echosens, Inventiva, LabCorp, and Nordic Bioscience. He is also a consultant for Aligos, Arrowhead, AstraZeneca, BMS, Boehringer Ingelheim, Covance, Eli Lilly, GSK, Madrigal, Novo Nordisk, Prosciento, Sagimet, and Siemens. J.S. has served as an advisor or consultant to Abbott, AstraZeneca, Bayer, Eli Lilly, Madrigal, Nova, and Novo Nordisk. No other potential conflicts of interest relevant to this article were reported.

AUTHOR CONTRIBUTIONS

All authors contributed to writing, reviewing, and editing the manuscript. K.C. is the guarantor of this work and, as such, had full access to all materials and takes responsibility for the accuracy and integrity of the content.

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