



A clinical decision support tool for metabolic dysfunction-associated steatohepatitis in real-world clinical settings: a mixed-method implementation research study protocol

Jesse Fishman¹, Theresa Alexander¹, Yestle Kim^{*,1}, Iris Kindt² & Patricia Mendez¹

¹Madrigal Pharmaceuticals, Inc., West Conshohocken, PA 19428, USA

²DEARhealth, Westlake Village, CA 91362, USA

*Author for correspondence: ykim@madrigalpharma.com

Aim: A clinical decision support (CDS) tool for metabolic dysfunction-associated steatohepatitis (MASH) was developed to align health systems with clinical guidelines detailed in the MASH Clinical Care Pathway and improve patients' proactive self-management of their disease. The tool includes a provider-facing web-based application and a mobile application (app) for patients. This protocol outlines a pilot study that will systematically evaluate the implementation of the tool in real-world clinical practice settings.

Materials & methods: This implementation research study will use a simultaneous mixed-methods design and is guided by the Consolidated Framework for Implementation Research. The CDS tool for MASH will be piloted for ≥ 3 months at multiple US-based sites with eligible gastroenterologists and hepatologists ($n = 5\text{--}10$ per site) and their patients ($n = 50\text{--}100$ per site) with MASH or suspected MASH. Each pilot site may choose one or all focus areas within the tool (i.e., risk stratification, screening and referral, or patient care management), based on on-site capabilities. Prior to and at the end of the pilot period, providers and patients will complete quantitative surveys and partake in semi-structured interviews. Outcomes will include understanding the feasibility of implementing the tool in real-world clinical settings, its effectiveness in increasing patient screenings and risk stratification for MASH, its ability to improve provider and patient knowledge of MASH, barriers to adoption of the tool and the tool's capacity to enhance patient engagement and satisfaction with their care. **Conclusion:** Findings will inform the scalable implementation of the tool to ensure patients at risk for MASH are identified early, referred to specialty care when necessary and managed appropriately. Successful integration of the patient app can contribute to better health outcomes for patients by facilitating their active participation in the management of their condition.

Plain language summary: Nonalcoholic steatohepatitis, also known as metabolic dysfunction-associated steatohepatitis, or MASH, is a disease where the liver becomes inflamed and damaged. If MASH is not caught early and managed properly, the liver can stop working normally and/or develop liver cancer. There are guidelines for diagnosing and treating MASH, but doctors do not always use them and the disease may not be caught in time. Many patients do not know about this disease or what they can do to manage it. We have developed an online tool for doctors and a mobile app for patients to learn about and manage MASH. The tool will be tested at hospitals, in clinics, and with patients to see how well it works to screen for and manage the disease. Participating doctors and patients will complete surveys so we can understand their experiences with the tool. If the tool works, it could be used by many different doctors to help them identify MASH and give patients better care. The mobile app could help patients feel empowered to make decisions about their disease.

Shareable abstract: Madrigal Pharmaceuticals, Inc., and DEARhealth, Inc., have developed a digital clinical decision support tool for NASH/MASH. The group has provided details about a pilot implementation study to assess the effectiveness and feasibility of the tool in real-world practice settings.

First draft submitted: 17 May 2024; Accepted for publication: 13 August 2024; Published online: 20 September 2024

Keywords: attitudes • digital health tool • evidence-based guidelines • health knowledge • medical software • metabolic dysfunction-associated steatohepatitis • mobile applications • nonalcoholic • patient compliance • practice • public health • steatohepatitis

Background

Nonalcoholic steatohepatitis (NASH), also known as metabolic dysfunction-associated steatohepatitis (MASH), is a growing public health problem with substantial economic and personal burden [1–4]. MASH affects ~4–6% of adults in the US and can progress to advanced fibrosis and cirrhosis in about 25% of patients [5,6]. Patients initially present with nonspecific symptoms, but worsening MASH increases morbidity and may progress to severe liver-related complications, including end-stage liver disease and the need for liver transplant [7–11]. Patients with MASH are at high risk of mortality, and cardiovascular disease is the leading cause of death in this population [12,13]. Many patients with MASH exhibit components of metabolic syndrome, including obesity, Type 2 diabetes and hypertension, that increases the risk of disease progression and mortality [9,14,15]. The at-risk population for MASH is expected to increase given the rising prevalence of metabolic syndrome and its components [4,15]. The economic burden of MASH is substantial, exceeding \$223 billion in lifetime direct medical expenses for US patients with MASH, and the costs escalate with advanced disease [16,17]. Patients with MASH also experience a significant health-related quality of life burden that increases with disease progression [18–20].

MASH care gaps

Key care gaps in MASH include challenges in diagnosis and screening, gaps in management and treatment and poor patient education and engagement. Effective diagnostic and management strategies are crucial to address the escalating impact of MASH on health systems and improve patient outcomes. The severity of liver fibrosis is the strongest predictor of all-cause mortality, liver-related morbidity and liver transplantation; primary risk assessment is important to identify patients with asymptomatic but clinically significant fibrosis (stage ≥ 2) [9,12]. Recent clinical practice guidelines recommend the use of noninvasive testing, such as the Fibrosis-4 (FIB-4) index and liver stiffness measurement by transient elastography for primary and secondary risk assessment [9,21,22]. Despite the existence of evidence-based guidelines for the screening, referral and management practices for MASH [23–26], the disease is still severely underdiagnosed [27]. This is partially explained by the presence of nonspecific symptoms, such as tiredness or pain in the upper right side of the abdomen, during the early stages of the disease [9,28] and exacerbated by physician knowledge gaps [29–33] and inconsistent adherence to screening guidelines [34–36]. An important challenge is that many noninvasive tests are often costly, with limited availability and inadequate reimbursement [37].

Identifying patients at risk for MASH is the important first step to connect them with lifestyle changes and treatments that can potentially prevent the long-term consequences of the disease [9]. Current guidelines recommend lifestyle modifications to manage the comorbidities associated with the disease [9,22]. Resmetirom, a thyroid hormone receptor- β agonist, is the first and only treatment approved by the US FDA for MASH. It is indicated in conjunction with diet and exercise for the treatment of adults with noncirrhotic MASH with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis) [38]. Resmetirom may be considered for patients with intermediate MASH (FIB-4: <1.3 ; ELF: 7.7–9.8; vibration-controlled transient elastography: 8.1–12; magnetic resonance elastography: 2.6–3.6) [21,22,39]. Continuous disease management and regular reevaluations are crucial for MASH; however, among patients with MASH without cirrhosis, less than 50% are assessed every 2–3 years as recommended by current guidelines [24,40]. Provider referral rates to hepatologists and gastroenterologists are low for patients with MASH [41,42]. Monitoring practices appear to differ across sites; one study reported an absence of monitoring practices among US hepatologists and gastroenterologists [27,41].

Several studies highlight the unmet need for patient engagement strategies that facilitate patients' proactive self-management of their chronic disease, which plays a crucial role in improving health outcomes and enhancing overall quality of life [43]. Patient knowledge and awareness of the disease, including among patients with high-risk comorbidities, is generally low. Patients with diagnosed MASH frequently report that the education and support provided by their physician are insufficient [20,28,44]. Additionally, online educational resources for patients are often lengthy and complex [45]. Inadequate patient knowledge and awareness of MASH may lead to patients dismissing their diagnosis or underestimating its severity, often perceiving it as mostly weight-related or believing weight is

Table 1. Overview of a MASH CDS tool.

Care gap	Description	Ref.
Risk stratification	Based on patient data integrated via Redox or entered manually by a member of the care team and other questionnaires, the MASH CDS tool will present a dashboard of patients ordered by risk level (low, intermediate, high) for MASH-related fibrosis	[23,24,48]
Screening and referral – intermediate risk patients are screened and referred to hepatology as needed	Based on the provider reviewed patient risk level, the MASH CDS tool will recommend secondary tests for patients with intermediate risk to determine the patients' needs for referral to hepatology or ongoing monitoring	[23,24,48]
Patient care management, engagement and follow-up specialty care	Based on the provider-reviewed patient risk level, the MASH CDS tool will recommend a patient care management plan and patient follow-up schedule including multidisciplinary care, lifestyle management, medication management, disease management and patient engagement	[9,23,24]
AACE: American Association of Clinical Endocrinology; AASLD: American Association for the Study of Liver Diseases; AGA: American Gastroenterological Association; CDS: Clinical decision support; MASH: Metabolic dysfunction-associated steatohepatitis.		

the sole driver of fibrosis progression [20]. This limited understanding can compromise efforts to adhere to regular monitoring and adopt lifestyle adjustments crucial to halting disease progression [46,47].

MASH CDS Tool on the DEARhealth Platform

Overall, there is a significant need in clinical settings for practical tools that enable providers to implement evidence-based guidelines and to accurately identify, refer and manage patients with MASH. Equally important is the need to enhance patient engagement strategies to improve patients' disease awareness, prompt timely screenings and facilitate proactive self-management of their disease outside of clinical settings. The integration of innovative technologies in healthcare systems offers promising avenues for addressing these challenges. In 2021, a machine learning model for MASH called NASHmap was developed as a risk stratification algorithm for care providers [48]. In addition, the AGA released a MASH Clinical Care Pathway app (<https://MASH.gastro.org/app>) for mobile devices in 2022 to assist practitioners in identifying, evaluating and managing patients with MASH. However, NASHmap has not been broadly implemented, and the MASH Clinical Care Pathway app lacks regular updates. Both tools are constrained by the absence of structured follow-up and monitoring plans for patients with MASH and the lack of a patient-facing component for disease education, capturing patient-reported outcomes and promoting active patient engagement in disease management.

Madrigal Pharmaceuticals, Inc. (PA, USA) partnered with DEARhealth (CA, USA) to develop a clinical decision support (CDS) tool for MASH on the DEARhealth platform. This software, comprising a provider-facing web-based application and a mobile application (app) for patients, was designed to offer solutions to care gaps in MASH risk stratification, screening and referral and ongoing patient management (Table 1) [24]. Unlike existing tools that lack structured follow-up and monitoring plans for patients with MASH, this tool provides a comprehensive framework for proactive care. Drawing from multiple evidence-based clinical guidance documents, the MASH CDS tool covers the end-to-end patient journey, from MASH risk assessment to disease monitoring and management. The web-based MASH CDS tool aims to align health systems with the MASH Clinical Care Pathway (Figure 1) by providing prompts and reminders that assist providers in implementing evidence-based clinical guidelines at the point of care. Clinical recommendations provided by the tool require independent evaluation by providers who retain the discretion to accept or reject such guidance. The CDS tool is designed with a user-friendly interface, making it more accessible to a broader range of healthcare providers, including those in primary care and endocrinology settings. Another novel feature of the tool compared with existing tools is its patient mobile app which includes functionalities aimed at improving patient engagement through access to educational resources and tools for self-monitoring and management. Patients may participate in patient history questionnaires, access educational resources on MASH through “My Academy,” and view their care pathway, suggested follow-up appointments and planned and completed activities. The mobile app enhances accessibility by providing real-time updates, personalized content, interactive features and educational resources that empower patients to manage their health conveniently and effectively.

Unfortunately, the implementation and adoption of innovative technologies for healthcare is known to be challenging [50–52]. Several institutions, including the US National Institutes of Health, prioritize research focused on the implementation and adoption of interventions in real-world settings [53–55]. By prioritizing practical utilization, these implementation research efforts aim to improve the acceptance and effectiveness of innovative healthcare

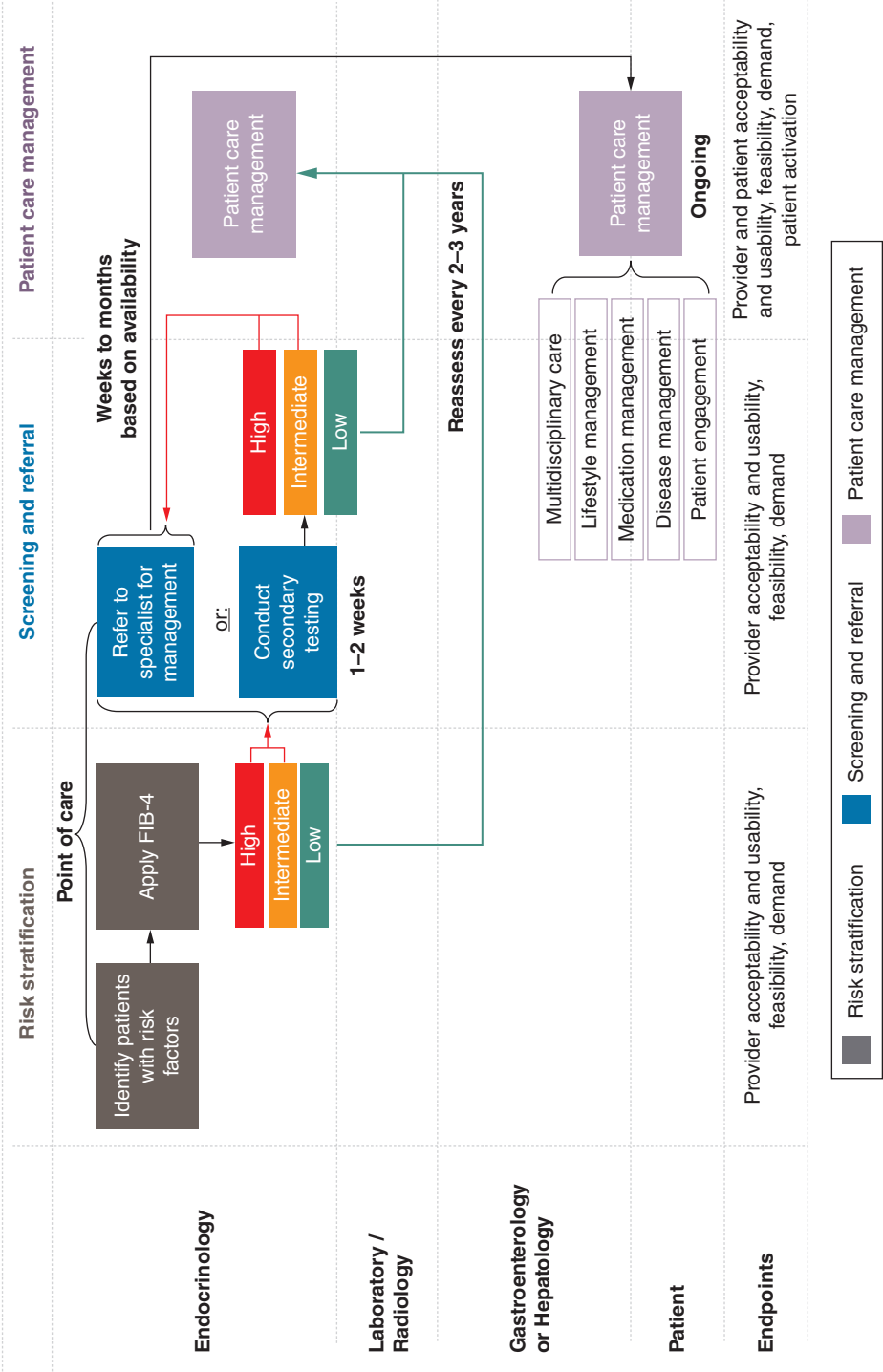


Figure 1. The MASH clinical care pathway.
FIB-4: Fibrosis-4 Index; MASH: Metabolic dysfunction-associated steatohepatitis.

solutions. Therefore, an empirical pilot study to evaluate the MASH CDS tool is important to assess the feasibility of implementation, identify barriers to acceptance and use of the tool in routine practice and determine the advantages of the tool to improve knowledge and influence behavior among providers and patients. Findings from such a study will guide approaches to guide widespread integration of the tool.

The majority of patients diagnosed with MASH are under the care of gastroenterologists/hepatologists and many patients with MASH are currently being missed in non-GI/hepatology settings, such as primary care and endocrinology. The ultimate goal of developing the CDS tool for MASH is to improve identification and referral of high-risk patients from these settings to specialized gastroenterology (GI)/hepatology care. This pilot study focuses on providers and patients in GI/hepatology settings to establish tool efficacy and feasibility, and the same protocol will be used to expand the program to additional clinical settings. Validating the effectiveness of the tool in specialist care could facilitate expanding its application to primary care and endocrinology settings, thereby enhancing referrals to specialty care and improving patient outcomes on a larger scale.

Objectives

Here we outline the protocol for an implementation research study employing a simultaneous mixed-methods design to determine the feasibility of implementing a MASH CDS tool in real-world GI/hepatology practice settings; examine whether use of the tool increases knowledge and confidence among clinical staff in identifying and/or managing patients at risk of MASH; identify barriers, facilitators and best practices for implementing the tool in clinical settings; and identify key aspects of the patient app that resonate with patients and optimize usability, engagement and satisfaction. A full list of objectives is provided in [Table 2](#).

Methods

Design

This pilot implementation research study will employ a simultaneous mixed-methods design, guided by determinant implementation research frameworks, including the Consolidated Framework for Implementation Research (CFIR) ([Supplemental Figure 1](#)) [49,56]. Mixed-methods research combines the strengths of both qualitative and quantitative approaches and allows for a comprehensive examination of the research objectives with flexibility and depth [57]; a simultaneous mixed-methods approach gives equal weight to both quantitative and qualitative data [58]. Determinant frameworks in implementation research outline the factors that may act as barriers or enablers to successful implementation [49]. The CFIR is one of the most widely used approaches to guide the evaluation of factors influencing the successful implementation of innovations within healthcare settings [56].

Prior to and at the end of the implementation period (a minimum of three months per site), providers will complete quantitative web-based surveys and patients will complete surveys in the mobile app. To complement breadth and expand the depth of understanding afforded by the quantitative survey data, semi-structured interviews will be conducted with providers and patients who have completed the pre- and post-implementation surveys and utilized the tools. Qualitative data analysis will follow an inductive approach.

The study is currently recruiting pilot sites, and data collection is expected to conclude in 2025. Findings will be reported in accordance with established guidelines for implementation and mixed-methods research [59,60].

Setting

The pilot study will be conducted at various US-based gastroenterology and hepatology sites, including both integrated gastroenterology and hepatology offices and those where these services operate separately. Referrals are not a focus of this pilot, which primarily aims to thoroughly evaluate the tool's effectiveness and adaptability in environments with specialized expertise and resources. Based on this assessment, we will adapt the tool for use in endocrinology and primary care environments considering differences in available resources, including the availability of noninvasive tests and biomarkers, to ensure the tool's utility across diverse healthcare settings. The study sites include a mix of academic centers and large institutions, chosen specifically for their high prevalence of MASH. Community-based, suburban and rural sites will not be included.

The study aims to target sites in the following categories: a health system or pilot site that currently does not have a way to screen or identify potential patients with MASH; a health system or pilot site that currently does have a way to screen or identify potential patients with MASH, but either does so sporadically or inadequately or may not adhere to additional components of guidelines, such as confirming that patients identified are appropriately referred or performing next steps of ultrasounds or other guideline-based tests; or a health system or pilot site that

Table 2. Study objectives, outcomes and methodology.

Target population	Objective	Method(s)
Providers [†]	1. To test whether an intervention consisting of a web- or app-based MASH CDS tool can be integrated into gastroenterology and hepatology settings and used to risk stratify, screen, refer, and/or manage patients at high risk or intermediate risk for MASH with clinically significant fibrosis	• Effectiveness of the tool to improve clinician knowledge of MASH diagnostic and/or treatment pathways • Changes from baseline in estimate of patients screened and identified as at risk for MASH in pilot sites • Changes from baseline confidence in identifying and/or managing patients with MASH (KACE) • HSUS score • Changes from baseline in extent and variety of symptoms experienced, and the effect of symptoms on activities and mood (CLDQ) • Qualitative interviews in which providers will be asked about the effect of the MASH CDS tool on patients' involvement in their own process
	2. To investigate feasibility of such a tool in clinical settings by a care team	• Changes from baseline in clinicians' views on the usability and feasibility of the MASH CDS tool ◦ HSUS score ◦ Feasibility of Intervention Measure (extent to which a new innovation can be successfully used or carried out within a given agency or setting) ■ Reported processes associated with implementation ■ Barriers to routinely incorporating the MASH CDS tool into clinical workflow
	3. To examine whether use of the tool increases knowledge and confidence among clinical staff in identifying and/or managing patients at risk of MASH	• Changes from baseline in clinicians' knowledge of/familiarity with MASH diagnostic and/or treatment pathways • Changes from baseline in clinicians' confidence in identifying and/or managing patients (KACE)
	4. To understand the barriers and facilitators for use of a MASH CDS tool and how these may vary between hepatology and gastroenterology	• Identification of clinician's specialty • Feedback on implementation and practicality of the MASH CDS tool in a clinical setting ◦ Level of effort required to use the tool ◦ Ability to complete each step without additional assistance ◦ Frequency of incomplete use of tool during patient interaction • Access to necessary information to follow the recommended care pathway • Open-ended questions on barriers and facilitators to using the tool
	5. To examine whether large-scale expansion and implementation of such a tool would be feasible	• Degree to which there is a stated need for an intervention and the extent to which the intervention meets that need (electronic medical record data and survey data) • Clinicians' view on appropriateness of the tool for further roll-out into clinical practice • NPS to determine whether staff would recommend the tool
	6. To inform best practices for implementing the MASH CDS tool in clinical practice and identify potential revisions or refinements to support usability and expanded use of the tool	• Clinicians' personal experiences of using the tool, including: ◦ Whether it includes all necessary information ◦ Identification of components that did not meet the clinical needs of clinicians • Qualitative interviews to gain clinicians' input on workflow and implementation strategies, including suggested standard operating procedures and modifications to improve the usability of the tool
	7. To assess the acceptability, usability and satisfaction of provider-facing aspects of the MASH CDS tool	• HSUS to assess usability of the system • Reported satisfaction with MASH CDS tool • Reported intent to continue use • Perceived value • Reported understanding of tool • NPS to determine whether staff would recommend the tool
Patients [‡]	1. To assess the acceptability, usability and satisfaction of patient-facing aspects of the MASH CDS tool	• Baseline patient history • Changes from baseline in patients' views on the usability and feasibility of the app • The extent to which patients are engaged with the application • Changes from baseline in extent and variety of symptoms experienced, and the effect of symptoms on activities and mood (CLDQ) • HSUS to assess usability of the system
	2. To understand the ability of the patient-facing module to 'activate' patients	• Changes from baseline in patient knowledge (Patient Decision Aids developed by the Ottawa Hospital Research Institute, revised for MASH) • Changes from baseline in PAM score to assess a patient's knowledge, skills and confidence managing their health and healthcare
	3. To understand the ability of the patient-facing module to enhance patient understanding of their disease, increase adherence to recommended care plans, and foster active participation in shared decision-making with healthcare providers	• Changes from baseline in PSQ-18 score

[†]For the pilot study, this refers specifically to the inclusion and exclusion criteria for the hepatologist or gastroenterologists who participate at each site. Other physicians (e.g., endocrinologists), clinical staff (e.g., nurse practitioners, registered nurses, medical assistants) and nonclinical staff (e.g., social workers, navigators, front desk staff, office managers) may be recruited in future.

[‡]Patients at risk for MASH and clinically significant MASH-related fibrosis.

CDS: Clinical decision support; CLDQ: Chronic Liver Disease Questionnaire; HSUS: Healthcare Systems Usability Scale; KACE: Knowledge, Attitudes, Access and Confidence Evaluation; MASH: Metabolic dysfunction-associated steatohepatitis; NPS: Net promoter score; PAM: Patient activation measure; PSQ-18: Patient Satisfaction Questionnaire-18.

Table 3. Provider and patient inclusion and exclusion criteria.

Providers [†]	
Inclusion criteria	Exclusion criteria
• Are one of: ◦ Gastroenterologist ◦ Hepatologist • Willing to / able to use the MASH CDS tool in clinical practice for at least 3 months • Have access to an internet-connected device with internet browsing function and email • Completed onboarding and training	
Patients	
Inclusion criteria	Exclusion criteria
• Aged 18 years or older • Willing to / able to use the MASH CDS app • Have access to an internet-connected device with internet browsing function and email • Are willing and able to read an informed consent form and provide consent to participate • May be at risk for MASH-related fibrosis	
Additional patient eligibility criteria	
Risk stratification • Patients aged 18 or older who may be at risk for MASH-related fibrosis, which may include: ◦ Adults with obesity, MetS, prediabetes, T2DM (even with normal liver enzyme levels), or T1DM (if other risk factors are also present), or ◦ Adults with hepatic steatosis on imaging studies	
Screening and referral – intermediate-risk patients are screened and referred to hepatology as needed • Patients aged 18 or older who are categorized as at intermediate risk for MASH-related fibrosis (stages F2–F4) according to their FIB-4 output (FIB-4 1.3 to 2.67)	
Patient care management, engagement and follow-up specialty care • Patients aged 18 or older who are categorized as at low, intermediate, or high risk for MASH-related fibrosis[‡] • Low risk: FIB-4 <1.3 for patients aged 36 to 64 years; FIB-4 <1.9 to 2.0 for patients aged 65 years or older; FIB-4 1.0 for patients with T2DM • Intermediate risk: FIB-4 1.3 to 2.67 for patients aged 36 to 64 years; FIB-4 2.0 to 2.67 for patients aged 65 years or older • High risk: FIB-4 >2.67 for patients aged 36 years and older	
[†] For the pilot study, this refers specifically to the inclusion and exclusion criteria for the hepatologists and gastroenterologists who participate at each site. Other physicians (e.g., endocrinologists), clinical staff (e.g., nurse practitioners, registered nurses, medical assistants) and nonclinical staff (e.g., social workers, navigators, front desk staff, office managers) may be recruited in future.	
[‡] Note that risk level can be applied through the use of the risk stratification and screening and referral aspects of the MASH Clinical Care Pathway or, if the site is only using the patient care management aspect of the MASH Clinical Care Pathway, the provider can set the patient's risk level. Low-risk patients are included below for reference, but the study will primarily focus on intermediate- and high-risk patients. The risk level for patients aged 18–35 will be determined by other noninvasive tests, due to the lack of accuracy of the FIB-4 in this age range as specified in the AASLD guidance.	
AASLD: American Association for the Study of Liver Disease; CDS: Clinical decision support; F: Fibrosis stage; FIB-4: Fibrosis-4 Index; MASH: Metabolic dysfunction-associated steatohepatitis; MetS: Metabolic syndrome; T1DM: Type 1 diabetes mellitus; T2DM: Type 2 diabetes mellitus.	

screens and identifies at-risk patients according to guidelines, but does not have a routine follow-up and patient management process (including annual HCC screening). Each pilot site has the flexibility to choose one or all focus areas within the MASH CDS tool (i.e., risk stratification, screening and referral or patient care management; [Figure 1](#)). This pathway will be tailored to the individual site based on the tools available onsite (e.g., FibroScan, ELF, etc.).

Participants

The study population will comprise eligible gastroenterologists and hepatologists and their patients with MASH or suspected MASH. Although the final sample size will depend on the number of providers and patients who are confirmed to participate at individual clinical sites, the research team aims to recruit 5–10 providers and 50–100 patients per site to participate in the study. Gastroenterology and hepatology specialties are well suited to manage ongoing care for patients due to their familiarity with care management plans for patients with a liver condition. Provider and patient inclusion and exclusion criteria are listed in [Table 3](#).

In contrast to conventional intervention research, which requires large sample sizes to ensure statistical power and generalizability, implementation research often necessitates substantially fewer participants. Typical sample sizes for implementation research range between five and ten individuals in key roles at each site, particularly for individual interviews [61]. This deliberate reduction in sample size enables a more focused and nuanced evaluation of the implementation process and its outcomes within the complexities of real-world clinical settings [62]. This focused approach facilitates a more comprehensive analysis of the implementation process, allowing for the identification of barriers, facilitators and contextual factors that influence intervention uptake and sustainability. In the current study, up to five providers and five patients per site (total of 10 participants per site) will participate in semi-structured interviews.

Procedures

Sites will implement the tool for a minimum of three months and site participation will end when one of two criteria are met: threshold of site staff recruited to participate in the study (ten users per site) or after the last patient enrolled completes the study (six months) (Supplemental Figure 1). Each pilot site will execute its implementation process independently from other sites.

At study initiation, each site will appoint a study site coordinator to oversee several key responsibilities. These include recruiting care team members, coordinating training sessions, ensuring adherence to the study protocol, managing the distribution and follow-up of data collection instruments, assisting with patient and provider interview recruitment and providing expertise on site-specific workflows. For sites without integrated electronic health record (EHR) systems compatible with the MASH CDS tool, the coordinator will support or arrange for manual data entry. Following care team recruitment, all participating providers and relevant pilot site staff will undergo an onboarding process. This will include virtual training to introduce the study, familiarize participants with the MASH CDS tool, and share best practices for implementing the intervention. A centralized coordination team will be responsible for overseeing onboarding and virtual training procedures across all study sites. This team will ensure consistent implementation and provide site support throughout the study.

Patient data to be used in the MASH CDS tool will be integrated via Redox for sites that choose to link their patient data. At some sites, the tool will operate independently of EHR systems, requiring providers to use it as a standalone application accessible via the Google Chrome web browser, which is commonly used in the workflows at the participating sites. Additionally, study coordinators may manually enter de-identified patient data into the DEARhealth platform. While the web browser approach may require some workflow adjustments, the tool is designed to be user-friendly and intuitive to minimize provider burden. Additionally, comprehensive training and support will be provided to facilitate smooth adoption and effective use in clinical practice. The DEARhealth implementation team will provide training and instructions covering the creation of provider accounts and patient profiles through connected EHR or manual entry. Pilot sites (providers and participating patients) will be able to receive additional support via DEARhealth support. During the implementation phase of the study, providers will use the MASH CDS tool to systematically stratify, screen, refer and manage patients at risk for MASH and MASH-related fibrosis, depending on their desired implementation, for approximately 3–6 months. After patient profiles are created by a designated person at each pilot site, patients at risk for MASH will be asked to provide written informed consent to participate in the study (either in person or virtually), after which they will receive email instructions to download the app.

Based on a combination of patient records and self-report questionnaires that include patient-reported outcomes data, providers will then complete a set of steps for fibrosis risk stratification. It is anticipated that hepatologists and gastroenterologists will perform screening and risk stratification procedures for patients referred from their primary provider and who have an unknown risk of liver fibrosis. In the pilot study, hepatologists and gastroenterologists will first use the MASH CDS tool as a guide to identify patients with risk factors for MASH-related fibrosis. They will then gather patient history and laboratory tests and apply a non-invasive test (e.g. FIB-4, FibroScan, magnetic resonance elastography) to determine the degree of liver fibrosis. For patients with intermediate risk for MASH, providers will conduct secondary testing to determine the need for ongoing follow-up. Patients at high risk for fibrosis based on high FIB-4 scores may either undergo secondary testing or be referred directly to specialized care, depending on the availability of testing resources in their setting. If secondary testing is available, it will be performed before referral; otherwise, patients will be referred directly. Providers may use a specific noninvasive test that is easily accessible to their practice and appropriate to the patient, thus not every pilot site will use the same noninvasive test. The providers will then review and approve the patient's risk level for liver fibrosis.

Based on the provider-approved patient risk level, the MASH CDS tool will recommend a care management plan and patient follow-up schedule. For patients at low risk of fibrosis, the provider will develop a plan for patient care follow-up, lifestyle management, medication management and patient engagement. For patients with high and intermediate risk, the provider will develop a patient care plan with recommendations for multidisciplinary care, lifestyle management, medication management, disease management and patient engagement to encourage patients to follow-up and monitor their disease progression with providers.

For sites that choose to integrate the MASH CDS tool with their EHR system, patient data will be transferred securely from the EHR system to the tool. De-identified data from each site will be exported from the tool and

securely transmitted to a central data coordination center for data validation prior to statistical analysis by a third party.

Outcomes

The intended outcomes of this study include the number of patients screened and identified as at risk for MASH in pilot sites, changes in scores from pre- to post-implementation in clinicians' and patients' perceptions regarding the usability and feasibility of the MASH CDS tool, and the effectiveness of the tool in improving clinician knowledge and adoption of MASH diagnostic and treatment pathways (Table 2). It is important that providers accurately identify and thoroughly evaluate patients before initiating treatment to ensure comprehensive care. Additional outcomes will include the effectiveness of the tool in enhancing patient understanding of their disease, increasing adherence to recommended care plans, and fostering active participation in shared decision-making with healthcare providers. This study also seeks to identify provider- and patient-related barriers to the adoption of the MASH CDS tool based on findings from both quantitative and qualitative methods.

Data collection

Digital surveys

Before the implementation of the MASH CDS tool, providers will receive a 15- to 20-min web-based survey comprising questions on general background information about the healthcare setting, and individual familiarity with diagnostic and/or treatment pathways in MASH. The survey will include a question, adapted from the Knowledge, Attitude, Access and Confidence Evaluation (KACE), on confidence in identifying and/or managing patients [61,63]. After implementation, providers will receive a 25- to 35-min survey about their experience using the tool and potential barriers for tool adoption. The survey will repeat many questions asked at baseline and will include two additional scores, the Healthcare Systems Usability Scale (HSUS) [64] and the Feasibility of Intervention Measure [65], and a question on whether staff would recommend the tool, which will be used to calculate a net promotor score (NPS) [66]. Qualitative questions will be included to elicit additional feedback.

Prior to and following the use of the app, patients will receive a 5- to 10-min survey via the mobile app comprising demographic questions, the HSUS [64] and the patient activation measure (PAM) [67]. The Patient Satisfaction Questionnaire-18 (PSQ-18) [68] and Chronic Liver Disease Questionnaire Version 4 (CLDQ4) [69] will be included as optional measures to collect disease-specific patient-reported outcomes.

The HSUS assesses the usability of a system or technology within healthcare settings [64]. Scores range from 0 to 100, with higher scores indicating better usability. The Feasibility of Intervention Measure evaluates the practicality and workability of implementing a specific intervention in a given context [65]. The scores for each question are converted, summed and multiplied by 2.5 to give an overall score from 0 to 100. Higher overall scores indicate greater feasibility, with 68 as an average score.

The PAM assesses a patient's knowledge, skills and confidence in managing their health and healthcare [67]. The PAM utilizes an externally validated and proprietary scoring algorithm to produce a PAM score along an empirical interval-level scale from 0 to 100, correlating to one of four levels of patient activation.

The PSQ-18 measures patient satisfaction with healthcare services [68]. Responses across seven domains (general satisfaction, technical quality, interpersonal manner, communication, financial aspects, time spent with doctor, accessibility and convenience) are scored on a Likert scale, and higher average scores indicate greater satisfaction.

The CLDQ4 assesses health-related quality of life in individuals with chronic liver disease, providing insights into the impact of the disease on various aspects of life [69]. Responses are scored across eight domains, and higher scores indicate better quality of life.

Qualitative methods

Understanding the barriers to adoption of the MASH CDS tool will be guided by Dissemination and Implementation Barriers and Facilitators Measurement Toolkit [70]. Individual in-depth interviews, using a structured interview guide, will be conducted with up to five providers and five patients (a total of 10 participants per site) who have completed the pre and post surveys and utilized the tool. This qualitative component specifically will allow participants to express their perspectives and experiences using the tool. Interviews will be audio-recorded and transcribed to facilitate data interpretation to better understand the impact of the tool on both the providers and patients.

Table 4. Potential barriers to the implementation of the MASH CDS tool.

Barrier domains of interest	Questions in the semi-structured interview guide
General	• Can you describe any problems or barriers that you faced in using the tool? • What did your practice do to overcome these barriers? What else could be done to overcome the identified barriers? • What kinds of changes did you have to make to your practice to implement the tool (e.g., changes in formal policies, changes to pre- or post-visit procedures, changes in care team composition)? • What are your thoughts about having this tool continue to be used in your clinical practice?
Attitudinal or rational-emotional barriers: Lack of efficacy, lack of confidence, lack of sense of authority, lack of outcome expectancy, lack of accurate self-assessment, cognitive, or attitudinal behaviors; lack of adherent or concordant behavior Cognitive-behavioral barriers: Lack of knowledge, awareness, professional skills, or appraisal skills Professional barriers: Influence of invariants such as age, experience, sex, lack of motivation, influence of individual characteristics, concern for legal issues, rigidity of professional boundaries, lack of appropriate peer influences or models	• How confident do you feel about the ability of using the tool in your practice beyond this pilot study? • How do you think other clinicians would feel about using the tool in their practice?
Barriers to practical use: Poor usability, problems with functionality, challenging implementation in real-world practice, limited perceived benefits of use	• Can you describe what you would modify to improve the tool's usability? • How did you optimize your own use of the tool with patients? • Over time, were there any differences in how you used the tool with the first patient and with later patients? • After using the tool, what is your perception of the quality of the supporting materials (training, support, etc.) provided to help you use the intervention? • How useful were the supporting materials provided as part of the study start-up for helping you to implement and use the intervention? • Can you describe any problems or barriers patients reported about using the tool? Please only share specific comments or feedback made by patients and not your perception or expectation of patient barriers • On a scale of 1–5, how challenging it was to use the tool in your practice, with 1 being easy and 5 being very difficult? • Can you describe how useful you believe the tool is in engaging patients in their treatment?
Barriers embedded in the guidelines or evidence: Lack of practical access, lack of clear structure, lack of utility, lack of local applicability, lack of convincing evidence	• Has there been a time when you disagreed with the recommendation from the tool? If so, can you describe why you deviated from the recommendation and the frequency of deviation?
Support or resources: Lack of support, lack of human and material resources, lack of financial resources or funding, lack of time	• Are there any policies or standard operating procedures that were needed to begin implementation of the tool? • Are there any health policy or organization documents required to begin implementation? • Can you describe the resources (staff, tablets, etc.) you used to implement the tool? • Did you use any other online resources for patient education? What is your process for directing patients to online resources? • Did you have sufficient resources to implement the tool within your clinic workflow? If not, what would better support the regular use of the tool?
System and process barriers: Lack of organization and structure, lack of harmony with health and oversight systems, lack of referral process, lack of workload-outcome balance, lack of teamwork structure and ethic	• Is there a designated team member who needs to approve the decision aid prior to implementation? • What staff members supported implementation of the tool? • If this were to be implemented outside of a research study, how would the process be different (i.e., what approvals would be necessary)? • Can you describe any processes within the practice that facilitated using the tool? • Can you describe any processes within the practice that facilitated use of the tool, as reported by patients? Please only share specific comments or feedback made by patients and not your perception or expectation of patient barriers. • At which points in the patient care journey do you think this tool would be helpful (e.g., at diagnosis, during initial treatment planning encounter, on an annual basis, etc.)? • Is there a patient population you wouldn't use this for?
CDS: Clinical decision support; MASH: Metabolic dysfunction-associated steatohepatitis.	

Data analysis

Closed-ended survey data will be summarized using descriptive analyses, including frequencies and means to assess feasibility domains and outcomes of interest. Open-ended survey responses and discussion narratives will be thematically summarized to provide an overall assessment of the workflow feasibility of the MASH CDS tool and the usability of the app. Pre- and post-implementation comparisons will be made using relevant statistical measures.

An established thematic analysis approach, similar to the method developed by Braun and Clarke, will be used to inductively identify thematic patterns from the interview data [71]. Coders will first familiarize themselves with the

narratives through multiple readings. Subsequently, a primary codebook will be developed through open coding of the data and categorization of codes based on similarities. These categories will then be organized into overarching themes that represent patterns within the data. Themes will undergo further refinement and definition. Finally, researchers will synthesize the overall significance and meaning of the emergent themes. A specific focus of the interviews will be to elicit information on the barriers to implementation of the MASH CDS tool (Table 4).

Discussion & conclusion

The development of a MASH CDS tool represents an important step forward to improve the screening, risk stratification and management of patients with MASH. Developed using evidence-based clinical guidelines outlined in the MASH Clinical Care Pathway, this tool aims to support healthcare providers in implementing these guidelines at the point of care. Unlike previous tools, the new tool integrates current treatment guidelines to provide a comprehensive framework for proactive care with detailed management and follow-up plans tailored to individual patient profiles. The tool features an intuitive interface designed for ease of use across various healthcare settings. Many existing decision support studies are focused on providers, but the MASH CDS tool includes a patient mobile app to complement provider efforts. By incorporating patient education and engagement features into the mobile app, this tool has the potential to empower patients to take a more active role in managing their condition, fostering better health outcomes and enhancing overall disease management [72,73].

This pilot study employs a simultaneous mixed methods design to comprehensively evaluate the feasibility and effectiveness of implementing MASH CDS tool in real-world clinical practice settings. By combining quantitative and qualitative approaches, this study aims to provide a comprehensive understanding of the implementation process and generate actionable insights to overcome barriers to implementation and guide the widespread integration of the tool into clinical practice. This pilot study focuses on GI/hepatology sites to ensure effective implementation of the tool among a population already familiar with MASH, thereby facilitating a controlled evaluation of its effectiveness before wider application. Understanding the feasibility for broader contexts, such as primary healthcare and endocrinology settings where early detection and initial management of MASH often occur, will require ongoing evaluation in these settings. Nevertheless, findings from this pilot study will inform improvements to the tool and provide insights for its scalable and sustained implementation in health systems. Efforts to identify and address key challenges regarding the adoption and usability of the tool are important to enhance the implementation process and ultimately improve healthcare delivery and patient outcomes.

Summary points

- Nonalcoholic steatohepatitis, also known as metabolic dysfunction-associated steatohepatitis (MASH), is a growing public health problem with substantial economic and personal burden.
- Practical tools are needed in clinical settings to help providers implement evidence-based guidelines and to accurately identify, refer and manage patients with MASH.
- Enhancing patient engagement strategies is also crucial to increase disease awareness, promote timely screenings and facilitate proactive self-management outside of clinical settings.
- A clinical decision support (CDS) tool for MASH was developed to align health systems with clinical guidelines and empower patients in self-managing their disease.
- This implementation research study will use a simultaneous mixed-methods design guided by the Consolidated Framework for Implementation Research.
- The CDS tool will be piloted for ≥ 3 months at multiple sites in the United States with eligible gastroenterologists and hepatologists ($n \leq 10$ per site) and their patients ($n = 50\text{--}100$ per site) with MASH or suspected MASH.
- Quantitative surveys and semi-structured interviews will be conducted with providers and patients before and after the pilot period to assess feasibility, effectiveness, knowledge improvement, barriers to adoption and patient engagement.
- Findings will inform the scalable implementation of the tool to ensure early identification, appropriate referral and management of patients at risk for MASH, potentially improving health outcomes through enhanced patient participation in disease management.

Supplementary data

To view the supplementary data that accompany this paper please visit the journal website at: <https://bpl-prod.literatumonline.com/doi/10.57264/cer-2024-0085>

Author contributions

J Fishman, T Alexander, Y Kim, I Kindt and P Mendez equally contributed to the study conception and design as well as the drafting and revision of the manuscript.

Acknowledgments

The authors thank IQVIA for executing the collection and analysis of provider survey data, as well as Avalere for support developing the study design and protocol.

Financial disclosure

This work was supported by Madrigal Pharmaceuticals, Inc. Publication costs were funded by Madrigal Pharmaceuticals, Inc. Jesse Fishman, Theresa Alexander, Yestle Kim, and Patricia Mendez are employees and shareholders of Madrigal Pharmaceuticals, Inc. Iris Kindt is a paid consultant for DEARhealth. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

Competing interests disclosure

The authors have no competing interests or relevant affiliations with any organization or entity with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

Writing disclosure

Medical writing and editorial assistance under the guidance of authors were provided by K Moxley and N Watson at ApotheCom, CA, USA and were funded by Madrigal Pharmaceuticals, Inc., PA, USA, in accordance with Good Publication Practice (GPP 2022) guidelines (*Ann Intern Med.* 2022; 10.7326/M22-1460).

Ethical conduct of research

This planned implementation research has been approved by the Western Institutional Review Board (WIRB)-Copernicus Group (WCG IRB), 23 April 2024. This study will be conducted in accordance with the principles of the Declaration of Helsinki and the International Council for Harmonisation Good Clinical Practice guidelines. The authors state that they have obtained institutional review board approval for the intended research. In addition, they will obtain verbal and/or written informed consent from the providers and patients who participate in this study.

Data sharing statement

No data were generated for this protocol manuscript.

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