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A European Survey to Identify Challenges in the Management of Metabolic Dysfunction-Associated Steatotic Liver Disease

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ABSTRACT

Background and Aims: Metabolic dysfunction-associated steatotic liver disease (MASLD) and its more severe subtype, metabolic dysfunction-associated steatohepatitis (MASH), are highly prevalent and strongly associated with obesity and type 2 diabetes (T2D). This study sought to identify challenges to the diagnosis, treatment and management of people living with MASLD and MASH and understand the key barriers to adopting relevant clinical guidelines.

Methods: A real-world, cross-sectional study (BARRIERS-MASLD) consisting of a quantitative survey and qualitative interviews of physicians in France, Germany, Italy, Spain and the United Kingdom was conducted from March to September 2023. Descriptive statistics were used for data analysis.

Results: A total of 626 physicians completed the survey; $n = 10$ from each country participated in the qualitative interviews. Physicians considered the presence of MASH to be highly impactful on how they treated people living with obesity (66%) and T2D (69%). Over one-third (35%) of the respondents could not identify any MASH-specific clinical guidelines issued by medical societies or associations top-of-mind, but overall awareness rose when prompted about country-specific guidelines. Physicians said they would need evidence of success (48%) and clinical guidelines that address common MASLD comorbidities (38%) to increase their adoption.

Abbreviations: AASLD, American Association for the Study of Liver Diseases; ADA, American Diabetes Association; EASD, European Association for the Study of Diabetes; EASO, European Association for the Study of Obesity; EASL, European Association for the Study of the Liver; FIB-4, fibrosis-4; FM, family medicine; GLP-1 RA, glucagon-like peptide-1 receptor agonist; GP, general practitioner; HCP, healthcare provider; IM, internal medicine; MASH, metabolic dysfunction-associated steatohepatitis; MASLD, metabolic dysfunction-associated steatotic liver disease; MP, metabolically focused physician; NAFLD, non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis; NIT, non-invasive test; T2D, type 2 diabetes; UK, United Kingdom; US, United States; VCTE, vibration-controlled transient elastography.

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Conclusions: This study found that lack of awareness around MASLD and MASH clinical guidelines and clearly established care pathways, particularly for addressing common comorbidities, was a key factor preventing physicians from optimising care for people living with MASH in Europe. This research highlights opportunities to improve education and training about clinical guidelines and care coordination.

1 | Introduction

Metabolic dysfunction-associated steatotic liver disease (MASLD), formerly known as non-alcoholic fatty liver disease (NAFLD) [1], is the most common chronic liver disease, with an estimated global prevalence of 38% among adults [2, 3]. Its more severe and progressive manifestation, metabolic dysfunction-associated steatohepatitis (MASH), formerly known as non-alcoholic steatohepatitis (NASH) [4], affects about 5% of the adult population worldwide, increasing up to 35% in those living with obesity and > 60% in those living with type 2 diabetes (T2D) [3–6]. Two systematic reviews estimated MASLD prevalence at approximately 25% among adults in Europe [3, 7], although estimates vary depending upon diagnostic method and the database source [3, 4, 7, 8].

The prevalence rates of MASLD and MASH are expected to increase along with those of obesity and T2D, making them a public health threat [8, 9]. The impact of metabolic risk factors on MASLD progression is well documented; other components of metabolic syndrome, like hypertension and hyperlipidaemia, are concomitant risk factors for extra-hepatic morbidity [3, 5, 10]. However, clinical guidelines set forth by several consensus groups and professional associations do not universally recommend assessing people living with metabolic risk factors for MASLD [11–15]. To better capture the metabolic aspects of the disease, in June 2023, multiple medical societies and patient advocacy groups specialising in liver disease published a global consensus statement on nomenclature revisions, replacing NAFLD with MASLD and NASH with MASH, which also aimed to remove the stigmatising nature of the terms ‘fatty’ and ‘alcoholic’ in the disease names [1].

Despite the existing guidelines for screening, diagnosing and managing MASLD [10, 12, 15], evidence suggests that they have not been widely adopted by healthcare providers (HCPs) in Europe [14, 16–18]. A 2020 qualitative study found various factors contributed to low implementation of clinical guidelines in diagnosing and managing MASLD, including HCP beliefs, attitudes, professional roles, knowledge, training, skills and environmental resources [18]. Although several clinically validated tools are recommended to confirm the presence of MASH and identify the disease stage, including liver biopsy and non-invasive tests (NITs) such as the Fibrosis-4 (FIB-4) index, Enhanced Liver Fibrosis test and vibration-controlled transient elastography (VCTE), when/which of these tools should be used varies, particularly in the presence of additional risk factors [19, 20].

Surveys have been a valuable tool in gaining insight into physicians’ use of clinical guidelines globally [18, 21–23]. This study aimed to understand physicians’ MASLD diagnosis and management practices, identify factors impacting earlier diagnosis

and optimised care and explore key barriers to adopting relevant clinical guidelines. This study also sought to assess multidisciplinary collaboration in the management of people living with MASH, including the perceived roles and expectations of different medical specialties.

2 | Materials and Methods

2.1 | Study Design and Ethical Approval

This cross-sectional study, BARRIERS-MASLD, included a quantitative survey and qualitative interviews of physicians and was conducted in France, Germany, Italy, Spain and the United Kingdom (UK) between 24 March and 12 September 2023. A total of 12 308 physicians were invited via email to participate in the study, recruited through online panel companies to which they had provided permission to be contacted for research purposes. Physicians who completed the survey and participated in the qualitative interviews received a modest monetary incentive.

The study was deemed to be exempt from review by the WCG Institutional Review Board (United States [US]), as the study included survey procedures with adequate provisions to protect the privacy of subjects and maintain data confidentiality. This study conformed to international ethical principles, including those of the Declaration of Helsinki.

2.2 | Survey Design

The survey, hosted online through the Decipher platform, was designed to (1) assess physicians’ roles, attitudes and experiences regarding diagnosing, treating and managing MASH; (2) assess awareness of MASH clinical guidelines and (3) understand perceived barriers and facilitators for relevant clinical guideline adoption. The survey instrument was developed by the authors and a third-party vendor (KJT Group Inc., Rochester, NY, USA) and can be found in the [Supporting Information](#). The survey was formulated in English and translated into the native language of each country. Pre-test interviews were conducted among a $n=10$ physicians in each country to assess the face validity of the survey; minor modifications were made to optimise its clarity and relevance.

The survey consisted of yes/no, single-choice, multiple-choice, open-ended numeric/text and Likert-scales, ranging from 1 (strongly disagree/not at all relevant/not influential at all/does not impact at all) to 7 (strongly agree/extremely relevant/extremely influential/greatly impacts). Because data collection started prior to the nomenclature change, the survey employed the terms NAFLD and NASH. However, the new nomenclature has been adopted in this article.

Summary

- Metabolic dysfunction-associated steatotic liver disease (MASLD) and its more severe form, metabolic dysfunction-associated steatohepatitis (MASH), are common liver diseases often affecting people with other diseases, such as obesity and type 2 diabetes (T2D).
- This study surveyed doctors in France, Germany, Italy, Spain and the United Kingdom in 2023 to ask about their experiences with patients with MASLD and MASH. Results showed that doctors believe that MASH affects their approach to treating patients with obesity and T2D. However, many were unaware of clinical guidelines for MASH and needed more evidence of successful treatments and guidelines that address common health issues related to MASH to follow these guidelines more closely.
- We concluded that doctors' lack of awareness about MASH guidelines and established treatment plans for patients with MASH limited their ability to provide optimal care. This demonstrates the need for better education, training and care coordination among physicians treating patients with MASH in these European countries.

2.3 | Participants

To be eligible for inclusion in the study, participants were required to belong to one of the following groups: (1) hepatologists or gastroenterologists with a sub-specialty in hepatology, collectively termed 'hepatologists,' who spent at least 50% of their time in an office or outpatient setting and saw ≥ 15 patients with MASLD per month; or (2) endocrinologists, general practitioners (GPs), family medicine (FM) or internal medicine (IM) physicians without a sub-specialty in hepatology who saw ≥ 15 patients with or suspected of having MASLD or MASH and treated ≥ 30 patients with T2D and/or obesity per month, collectively termed 'metabolically focused physicians (MPs)' for the purposes of this study. Both groups were required to have been in their role for at least 3 years and spend at least 60% of their time in direct patient care. The number of patients and proportions of time were self-reported by potential participants at screening. Physicians' practice locations were defined in four categories using definitions based on previous research in the same European countries [24]. Respondents consented to participate in the study and were informed their participation was voluntary and could be discontinued at any time.

2.4 | Qualitative Interviews

After survey completion, we asked participants about their desire to participate in further research and to be contacted for qualitative interviews. The 45-min interviews were moderated by a native speaker using a discussion guide to gain additional insights. Additional topics included collaboration with other specialties, awareness of the new steatotic liver disease nomenclature and attitudes towards clinical guidelines.

2.5 | Statistical Analyses

Descriptive statistical analyses (means and frequencies) of the aggregated quantitative data were performed using Q Research Software for Windows (a division of Displayr Inc., New South Wales, Australia). Tests of differences (chi-square test and *t*-tests) within respondent types were performed using Q Research Software tables. Statistical significance was set at $p < 0.05$, using two-tailed tests. Data are presented as numbers and percentages for categorical variables, and continuous data are expressed as the mean \pm standard deviation (SD) unless otherwise specified. The qualitative data analysis included coding the transcripts to identify emerging themes and constructs. In describing the qualitative data, the following terms were used: 'most' when referring to $\geq 75\%$ of participants; 'many' when referring to $> 50\%$ of participants; 'several' when referring to $\sim 50\%$ of participants; 'some' when referring to $< 50\%$ of participants; 'few' when referring to no more than three participants and a 'couple' when referring to no more than two participants.

3 | Results

3.1 | Sample Characteristics

Of 2190 physicians responding to the survey invitation, 125–126 participants from each country completed the online survey. The remaining did not qualify, did not meet screening criteria or were over quota. Of 1300 physicians invited to the qualitative interviews, $n = 10$ from each country participated.

Of the 626 respondents completing the survey, the mean age was 52.1 years, mean time in practice was 20.3 years and most practiced in public settings (Table 1). The mean number of patients seen per month who were suspected of having or confirmed to have MASLD or MASH reported by hepatologists was higher than that reported by MPs (mean 151.8 vs. 117.6, respectively).

3.2 | Screening and Diagnosis of Patients With MASH

Physicians reported that 24% of their patients had a definitive diagnosis of MASH confirmed through biopsy, 56% had diagnoses made based on other diagnostics such as bloodwork and imaging, and 20% of patients were clinically suspected but not confirmed. The percentage of patients with confirmed MASH through biopsy reported by hepatologists was higher than the percentage reported by MPs (32% vs. 19%, respectively, $p < 0.05$). The percentage of HCPs reporting the clinical tests they use to profile patients suspected of having MASH and help confirm a MASH diagnosis is shown in Figure 1. Ultrasound, lipid levels and VCTE were the methods most often mentioned by physicians for profiling purposes, whereas VCTE and liver biopsy were most commonly used to confirm diagnosis.

Many physicians participating in the qualitative interviews confirmed that they used NITs rather than biopsy to identify fibrosis risk for at least 90% of their patients suspected of having MASH. According to one hepatologist '*...We do very few*

TABLE 1 | Participant characteristics (N=626).

Characteristics of survey respondents	All physicians (N=626)	Hepatologists (n=250)	MPs (n=376)
Mean age, years (SD)	52.1 (9.8)	51.0 (9.7)	52.8 (9.8)
Mean time in practice, years (SD)	20.3 (8.1)	18.8 (6.6)	21.2 (8.8)
Primary medical specialty, n (%) ^a			
Hepatology	114 (18)	114 (46)	—
Gastroenterology	118 (19)	118 (47)	—
Endocrinology	154 (25)	—	154 (41)
General practice/family medicine	174 (28)	—	174 (46)
Internal medicine	66 (11)	18 (7)	48 (13)
Practice setting, n (%)			
Public	525 (84)	225 (90)	300 (80)
Private	101 (16)	25 (10)	76 (20)
Primary practice location, n (%)			
Rural (< 10 000 people)	38 (6)	4 (2)	34 (9)
Small town (10 000–100 000 people)	139 (22)	44 (18)	95 (25)
Medium city (100 000–500 000 people)	211 (34)	88 (35)	123 (33)
Large city (> 500 000 people)	238 (38)	114 (46)	124 (33)
Mean number of patients with diagnosed or suspected MASLD/MASH seen per month, n (SD)	131.2 (104.3)	151.8 (117.3)	117.6 (92.4)
Mean percentage of patients with diagnosed or suspected MASLD/MASH with common comorbidities (top 6 most common conditions listed)	n = 617	n = 248	n = 369
Obesity	48	41	54
Dyslipidaemia	41	34	46
Type 2 diabetes	37	28	43
Hypertension	36	30	40
Hypertriglyceridemia	32	26	37
Cardiovascular disease	27	23	30

Abbreviations: MASLD, metabolic dysfunction-associated steatotic liver disease; MASH, metabolic dysfunction-associated steatohepatitis; MP, metabolically focused physician; SD, standard deviation.

^aNumbers may not sum to 100 due to rounding.

biopsies, except for research or clinical trials...with FibroScan and FIB4 we are able to determine the diagnosis in 95% of cases—when there is discordance between both tests, we will confirm with liver biopsy. In the absence of, or prior to, a biopsy, physicians reported that the presence of comorbidities such as obesity, metabolic syndrome and T2D often raised suspicion about the presence of MASH. This was reflected in the survey finding that patient comorbidities were considered the most impactful factor influencing physicians' approach to diagnosing MASH (61%).

The survey respondents were asked how they approached patients with MASH and certain comorbidities. Nearly two-thirds of physicians reported routinely screening for T2D (65%) and metabolic syndrome (64%) in patients with MASH. Hepatologists

were slightly more likely than MPs to screen for T2D (69% vs. 62%); screening for metabolic syndrome was similar for MPs and hepatologists (65% and 62%, respectively).

3.3 | Attitudes and Approaches Towards Treatment and Management of MASH

MPs reported initiating treatment for patients more frequently in earlier rather than later stages of fibrosis and referring patients to someone else for treatment in later stages; conversely, hepatologists were more likely to initiate treatment regardless of fibrosis stage (Figure 2). Physicians treating patients for MASH (n=497) recommended lifestyle changes focused on exercise for 75% of their patients with MASH and diet for 66% of their

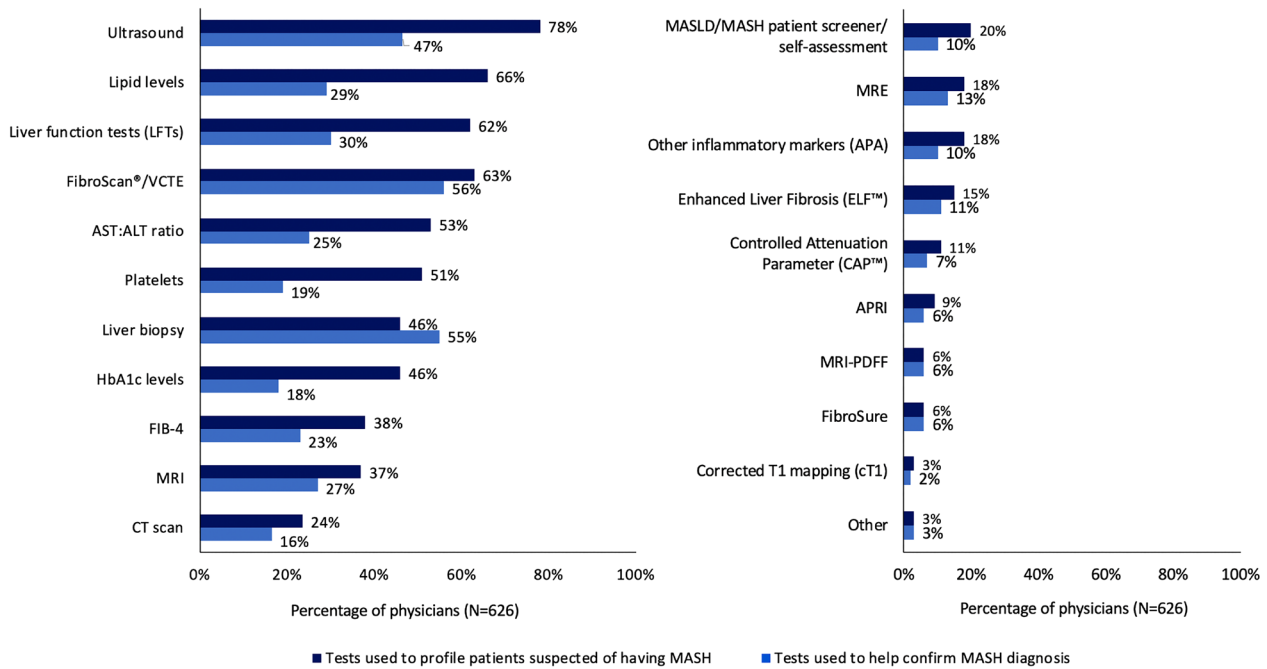


FIGURE 1 | Percentage of respondents ($N=626$) who said they used certain tests to profile patients suspected of having MASH and to help confirm a diagnosis of MASH. APRI, aspartate aminotransferase-to-platelet ratio index; AST:ALT, aspartate aminotransferase to alanine aminotransferase ratio; CT, computed tomography; FIB-4, fibrosis-4 index; HbA1c, glycated haemoglobin; MASLD, metabolic dysfunction-associated steatotic liver disease; MASH, metabolic dysfunction-associated steatohepatitis; MRE, magnetic resonance elastography; MRI-PDFF, magnetic resonance imaging—proton density fat fraction; VCTE, vibration-controlled transient elastography.

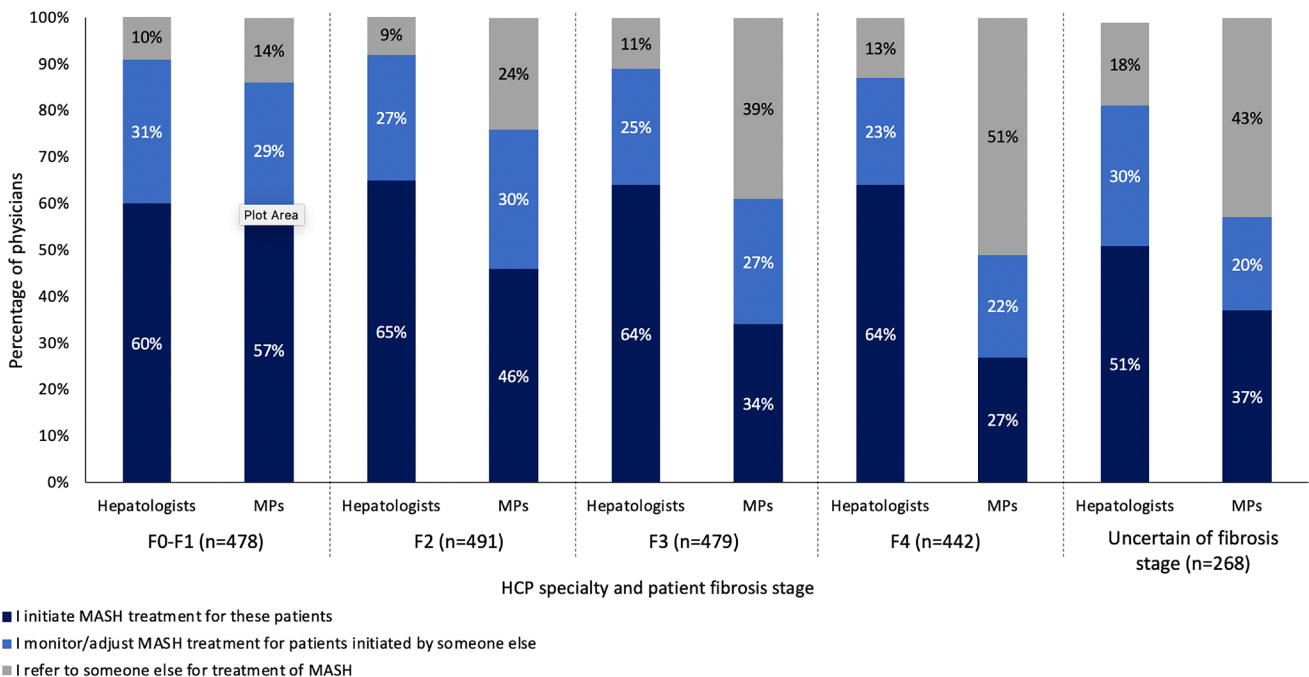


FIGURE 2 | Percentage of patients with MASH in various fibrosis stages for whom treatment is initiated, monitored/adjusted or referred to another healthcare provider, as reported by hepatologists and metabolically focused physicians. HCP, healthcare provider; MPs, metabolically focused physicians; MASH, metabolic dysfunction-associated steatohepatitis.

patients with MASH. Metformin and glucagon-like peptide-1 receptor agonists (GLP-1 RAs) were likely to be recommended for a greater proportion of MPs' patients with MASH than hepatologists' (34% vs. 23% and 28% vs. 19%, respectively, $p < 0.05$).

Many respondents considered the presence of MASH highly impactful on how they treated patients with T2D (69%) or obesity (66%). The likelihood of using pharmacologic treatments was relatively high when considering these comorbidities (Figure 3).

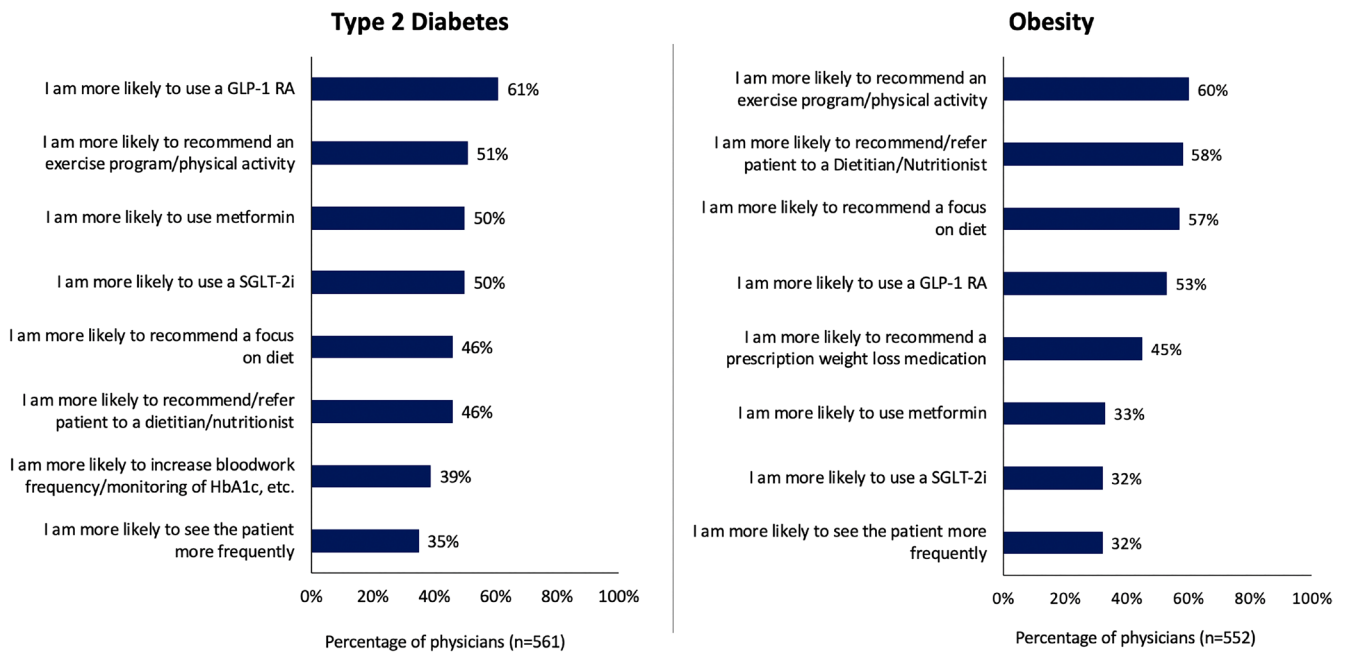


FIGURE 3 | Impact of the presence of MASH on treating a patient with type 2 diabetes and obesity. Based on those who answered 5, 6 or 7 on a 7-point scale where ‘1’ meant ‘doesn’t impact at all’ and ‘7’ meant ‘greatly impacts.’ HbA1c, glycated haemoglobin; GLP-1 RA, glucagon-like peptide-1 receptor agonist; SGLT-2i, sodium-glucose cotransporter-2 inhibitor; T2D, type 2 diabetes.

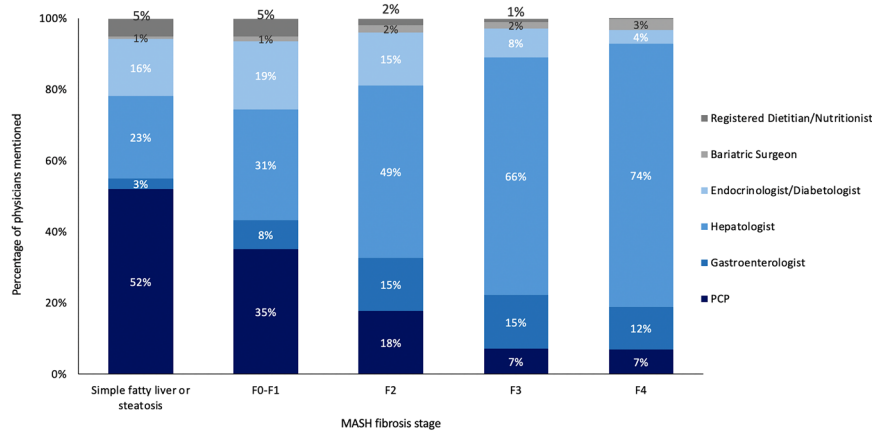


FIGURE 4 | Healthcare providers whom respondents ($N=626$) considered to be the coordinator of care for patients with different stages of MASH. MASH, metabolic dysfunction-associated steatohepatitis; PCP, primary care provider.

MPs were more likely than hepatologists to use a GLP-1 RA in a patient who has T2D (66% vs. 53%, $p < 0.05$) and obesity (61% vs. 41%, $p < 0.05$).

3.4 | Physician Roles, Responsibilities and Care Coordination for Patients With MASH

Surveyed physicians were asked about the care of patients with MASH across their respective countries beyond their practice and the patients they cared for. Most respondents identified hepatologists as those both currently and ideally responsible for diagnosing MASH by defining the fibrosis stage (89% and 86%, respectively), as well as those currently and ideally responsible for determining the initial course of treatment for MASH (86% and 82%, respectively). However, fewer saw hepatologists

as responsible for educating patients about MASLD and MASH (55% currently and 43% ideally). More than half of the respondents saw GP/IM/FM physicians as responsible for identifying patients at risk of MASLD or MASH (64% currently and 63% ideally) but not as responsible for patient education (47% currently and 42% ideally).

Hepatologists were seen as the specialty most responsible for coordinating care for patients with advanced MASH (F3-F4), but there was less consensus for patients with earlier stages of the disease (Figure 4). Qualitative discussions with physicians revealed that some felt communication between specialties could be improved to facilitate collaboration in managing patients with MASH. Roughly half (55%) of respondents reported referring to at least some patients with MASH to another HCP for ongoing treatment and management; more MPs than

hepatologists reported making referrals. Of the patients referred, 34% were referred to a dietitian/nutritionist, 31% to a hepatologist/another hepatologist and 19% to a gastroenterologist/another gastroenterologist.

3.5 | Awareness of/Attitudes Towards Guidelines for MASLD and MASH Management

When asked to think of clinical treatment guidelines top-of-mind (unprompted) for the diagnosis, treatment or management of MASH, 35% of survey respondents could not identify any guidelines issued by medical societies or associations on an international, national or local level. When provided with a list, approximately one-third of major society guidelines were recognised (Figure 5). Hepatologists were most aware of European Association for the Study of the Liver (EASL) 2021 (55%), American Association for the Study of Liver Diseases (AASLD) 2023 (44%) and AASLD 2018 (42%) guidelines. MPs were most aware of American Diabetes Association (ADA) (34%), ADA/European Association for the Study of Diabetes

(EASD) Consensus 2022 (28%) and EASL/EASD/European Association for the Study of Obesity (EASO) 2016 (25%) guidelines. These did not necessarily align with what respondents considered the most relevant (Figure 5). Conversely, country-specific guidelines were most recognised and considered the most relevant (Figure 5). Additionally, 4% of hepatologists and 16% of MPs were still unaware of MASH guidelines, even when prompted.

Published national and international clinical guidelines were considered highly impactful in diagnosing MASH for 49% and 48% of respondents, respectively, and treating MASH (54% and 52%, respectively). Although few (3%) disagreed (rating 1 or 2 on a 7-point scale) that following clinical guidelines improves patient outcomes, only about half (51%) strongly agreed (rating a 6 or 7). Fewer (44%) agreed that they almost always follow guidelines for the conditions they treat.

Physicians cited several factors related to diagnosing, treating and managing MASH preventing them from adopting clinical guidelines; however, more than one-third stated that there was

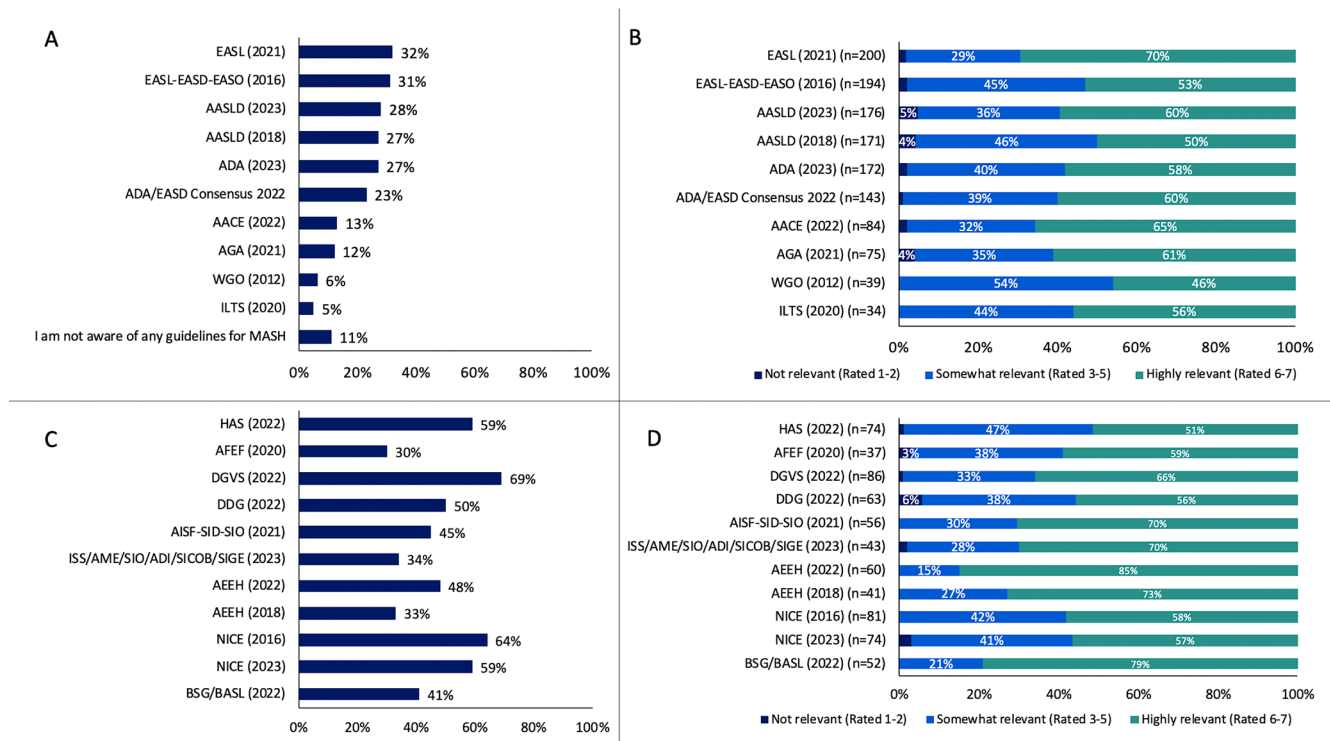


FIGURE 5 | (A) Aided awareness of international guidelines; (B) level of relevance of guidelines for the diagnosis, treatment, and management of MASH in practice; (C) aided awareness of country-specific guidelines; (D) level of relevance of country-specific guidelines for the diagnosis, treatment, and management of MASH in practice. Rated on a 7-point scale where '1' meant 'Not at all relevant' and '7' meant 'Extremely relevant' (N= 626). AACE, American Association of Clinical Endocrinology; AASLD, American Association for the Study of Liver Diseases; ADA, American Diabetes Association; AEEH, Asociación Española para el Estudio del Hígado; AFEF, Association Française pour l'Étude du Foie; AGA, American Gastroenterological Association; AISF-SID-SIO, Associazione Italiana per lo Studio del Fegato, Società Italiana di Diabetologia and Società Italiana dell'Obesità; BSG/BASL, British Society of Gastroenterology/British Association for the Study of the Liver; DDG, Deutsche Diabetes Gesellschaft; DGVS, Deutsche Gesellschaft für Gastroenterologie, Verdauungs- und Stoffwechselkrankheiten; EASL, European Association for the Study of the Liver; EASD, European Association for the Study of Diabetes; EASO, European Association for the Study of Obesity; HAS, Haute Autorité de Santé; ILTS, International Liver Transplantation Society; ISS/AME/SIO/ADI/SICOB/SIGE, Istituto Superiore di Sanità, Associazione Medici Endocrinologi, Società Italiana dell'Obesità, Associazione Italiana di Dietetica e Nutrizione Clinica, Società Italiana di Chirurgia dell'Obesità e delle malattie metaboliche, Società Italiana Gastroenterologia ed. Endoscopia Digestiva; NICE, National Institute for Health and Care Excellence; WGO, World Gastroenterology Organisation.

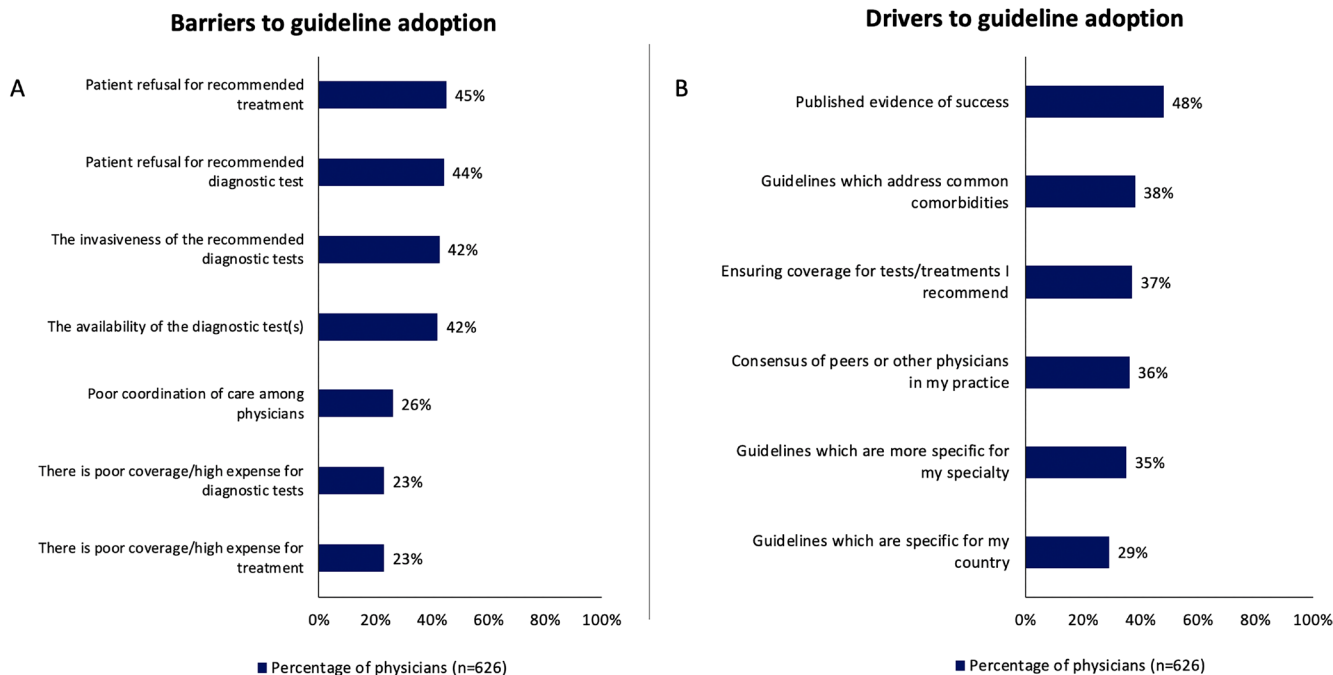


FIGURE 6 | (A) Factors related to the diagnosis, treatment and management of MASH that pose a barrier to adoption of clinical guidelines for physicians; (B) drivers to adoption of clinical guidelines. MASH, metabolic dysfunction-associated steatohepatitis.

nothing that would prevent them from adopting guidelines for MASH (Figure 6). More MPs than hepatologists (47% vs. 33%, $p < 0.05$) stated that the availability of diagnostic tests was a barrier to adopting guidelines related to treating MASH.

To consider adopting clinical guidelines, physicians need published evidence of success and guidelines that address common comorbidities (Figure 6). Specific evidence of success identified in a follow-up open-text question included outcomes/benefits (43%) or sample/study characteristics (38%). A smaller proportion stated that support from key opinion leaders (28%) and the willingness of other healthcare professionals to coordinate care (27%) would drive them to adopt clinical guidelines. When compared with MPs, hepatologists considered guidelines specific to their country (34% vs. 25%, $p < 0.05$), support from key opinion leaders (34% vs. 24%) and incentives to adopt clinical guidelines (26% vs. 17%, $p < 0.05$) to be greater drivers to adoption.

3.6 | Qualitative Findings Related to Nomenclature Change and Clinical Guidelines

In the qualitative interviews, participants were asked about the new MASLD and MASH nomenclature. Nearly half were aware of the new terms and stated that the nomenclature would not impact their approach to screening, diagnosing, or treating patients. More MPs than hepatologists reported being unaware of the new nomenclature. Some participants stated that the new nomenclature provided clearer and more precise definitions, was more accurate by including the term ‘metabolic’ and eliminated stigma by removing the word ‘alcohol’. As one hepatologist stated, ‘It is a more comprehensive nomenclature because we are talking about a metabolic syndrome and not just a liver condition. It also represents the current and

future management of the patient because we are talking about a metabolic and multidisciplinary approach—not just hepatology. It is a more modern definition of what is a condition that was already considered this way, but is now recognised in these terms’. According to another hepatologist, ‘New nomenclature is beneficial as it eliminates the stigma and ... the mention of alcohol, so we go from a negative definition to a positive definition that is associated to the metabolic risk factors. It allows to separate the different etiologies, which makes patient classification clearer’.

Some participants reported not following guidelines for diagnosing MASH and that promotion of clinical guidelines by scientific associations and organisations would help with adoption. Others said that they would like to see more interdisciplinary education and collaboration in the development of guidelines. As stated by one MP, ‘I think establishing a consensus among different specialties, more general guidelines. That in terms of scientific societies and then to make them known, I think congresses, forums and through courses’. Some respondents also stated that the guidelines need to be updated with the anticipated introduction of new therapeutic options to treat MASH.

4 | Discussion

This five-country study of physicians in Europe found widespread variability in the awareness and application of clinical practice guidelines for the diagnosis, treatment and management of MASLD and MASH. Most physicians agreed that published guidelines are important for diagnosing and treating patients with MASH, but some were unaware of any clinical guidelines. Notable differences were seen between hepatologists and MPs in the use of liver biopsy to diagnose MASH and the

use of pharmacologic treatments for patients with MASH, particularly when considering MASH in the presence of comorbidities such as T2D and obesity.

Although many guidelines do not have established standards for referral or treatment and care of patients with MASH and certain risk factors [14], physicians in this study consistently found patient comorbidities, especially cardiometabolic comorbidities, to be the most important factor impacting how they treat MASLD and MASH. There is a paucity of national strategies and public health-related policies for addressing MASLD and MASH across Europe [13, 14, 17, 25]. A lack of established clinical care pathways often creates confusion about how patients are referred to specialists and monitored for disease progression [14].

Our study aligns with previous research assessing the role of HCPs in diagnosing and treating patients with MASH. A patient journey study in the United States found that among 226 HCPs treating patients with MASH (75 of whom were hepatologists or gastroenterologists), a subset (12%) was similarly unaware of clinical guidelines for MASH, and 11% claimed not to follow any guidelines for the diagnosis of MASH [26]. However, the use of certain clinical tests to confirm MASH diagnosis varied when compared with HCPs in this study, with more US HCPs using liver function tests, ultrasound and VCTE [26].

This study supports other research reporting a lack of alignment between clinical practice guidelines issued by specialty societies and physician practice [16, 27], indicating that a multifactorial approach is needed to increase adoption by physicians caring for patients with MASH across Europe. Identifying potential barriers to using guidelines in clinical practice can improve adherence [22, 23]. One study found that lack of education or training, overly broad recommendations and discordance in guidelines on the same topic were barriers to adoption; therefore, guidelines tailored to these needs have a higher likelihood of implementation [22]. Similarly, a systematic review found that the most common barriers were lack of clarity in guidelines, guidelines conflicting with practice and insufficient evidence to support guidelines [28]. The review concluded that public policy improvements and removing common barriers in the healthcare system (e.g., time, available resources, etc.) could benefit increased implementation in practice [28].

For MASLD, assessing for fibrosis is an important benchmark for lifestyle changes that can facilitate reduced disease progression. One large ($n=2946$) prospective study found more than one-third of participants at risk of MASLD reported improving their diet and/or exercise habits within 6 months of being assessed for fibrosis, resulting in weight loss [29]. Similarly, early detection of MASLD is advantageous for individual and public health, as it is a prerequisite for early interventions. Further, one study found that a lack of knowledge about fibrosis stage among patients with MASLD correlated with poor adherence to lifestyle changes, particularly among those with obesity [30].

Although we found that two-thirds of patients were recommended lifestyle changes focusing on diet as a treatment for MASH, others have shown that physicians are generally not well-trained in nutrition education [11, 31]. Only 34% of

physicians referred to a dietitian or nutritionist; however, more than half were likely to recommend or refer a patient to another HCP when the patient had MASH and needed obesity treatment.

GPs in our study were largely viewed as responsible for identifying patients at risk of MASLD or MASH, but there was a lack of consensus about the responsibility for educating patients. In the United Kingdom, NICE 2016 guidelines for NAFLD assessment and management emphasise that primary care providers play an important role in identifying patients at high risk of developing MASLD and screening them for advanced liver disease [32]. However, the guidelines also recognise the limitations because such assessment requires physicians to be knowledgeable about MASLD and, in turn, educate patients about inherent risks of disease progression [18, 32]. This suggests that patients may not be receiving proper education about how to reduce their risk of developing MASLD or MASH, particularly when they have pre-existing cardiometabolic conditions. Improving HCP education about MASLD and MASH would, therefore, benefit patients by helping to mitigate risk factors that exacerbate the diseases.

The rising prevalence of obesity, T2D and metabolic syndrome is anticipated to create a subsequent rise in diagnosed cases of MASLD and MASH, impacting HCPs and countries offering resources to treat them [16, 33, 34]. People with MASLD who are detected early and offered nutrition and weight loss interventions may be able to decrease their risk factors or even reverse steatosis or fibrosis [33]. HCPs who use early interventions for patients with T2D or obesity at risk of MASH, such as lifestyle modifications or medications such as GLP-1 RAs or metformin, may prevent disease progression, lowering healthcare resource utilisation and the subsequent burden of disease [5]. Additionally, with the approval of the first MASH-specific drug in the United States, and expected approval in Europe in 2025, it is important to reach patients before their condition is irreversible [35]. Our study showed that MPs initiate treatment in earlier stages of fibrosis for patients with MASH, suggesting they may be best suited to optimise obesity- and diabetes-specific treatment for patients with MASH and comorbidities before they progress to advanced stages of steatosis.

4.1 | Limitations

The self-reported and non-probabilistic nature of this research offers several limitations. First, recall bias may have been a factor, particularly for questions regarding clinical guideline awareness. This was mitigated by first asking physicians to identify guidelines top-of-mind. Second, physicians were required to spend a certain amount of time in direct patient care. Therefore, our findings may not be entirely generalisable to a broader population of physicians who treat a larger or smaller proportion of patients. Similarly, the overall response rate of 18% and potential demographic differences between survey responders and non-responders may limit generalisability. Third, the survey did not evaluate physicians' patient population of those with MASLD or MASH via a chart review; therefore, there may be selection bias regarding the degree of MASH among their patients. Lastly, because few respondents were from rural areas, we cannot draw conclusions about the geographic availability of physicians and access to treatments.

5 | Conclusions

Physicians treating patients with MASLD and MASH are challenged by lack of diagnostic tools, established clinical care pathways and clinical guidelines addressing common comorbidities. While recommendations, approaches and models of care exist, gaps in knowledge and behaviour across specialties and countries may leave many patients with MASLD undiagnosed or with sub-optimal clinical management. Findings from this study emphasise a need for enhanced coordination of care, improved education about evolving clinical guidelines and opportunities for additional training about best practices for the integrated management of patients with MASH. In particular, established clinical care pathways for the treatment and care of patients with T2D and obesity should be leveraged as an opportunity to provide effective management for patients with MASH.

Author Contributions

All authors contributed to manuscript drafts, critically reviewed and approved the final manuscript and agreed upon the journal target. Specifically, L.C., W.A., E.B., C.C., M.F., M.R.G., J.M.S. and J.V.L.: writing – review and editing. R.B., P.P. and D.E.: conceptualisation, funding acquisition, supervision and writing – review and editing.

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Consent

All participants consented to participate in the research study.

Conflicts of Interest

Laurent Castera: Consultant for Boston Pharmaceutical, Echosens, Gilead, GSK, Madrigal, MSD, Novo Nordisk, Pfizer, Sagimet Biosciences and Siemens Healthineers; speaker honoraria from Echosens, Gilead, Inventiva Pharma, Madrigal and Novo Nordisk. William Alazawi: Advisory and speaker fees from GlaxoSmithKline, Novo Nordisk, Intercept, Thriva, Janssen, Gilead Sciences, Metadeq and UCB; competitive grant funding from GlaxoSmithKline, MSD and Gilead Sciences; director at Kudu Spectrum. Elisabetta Bugianesi: Consultant for Boehringer Ingelheim, Gilead Sciences, Intercept Pharmaceuticals, Inventiva Pharma, MSD, Novo Nordisk and Pfizer; research funding from Gilead Sciences and speaker honorarium from MSD, Novo Nordisk and Pfizer. Cyrielle Caussy: Consultant for Novo Nordisk, Bayer, Lilly, E-Scopics, Echosens, AstraZeneca and Pfizer; speaker honoraria from Echosens, Novo Nordisk, Madrigal, E-Scopics, Lilly and Astra Zeneca and research grants from Gilead Sciences, Novo Nordisk and Echosens. Massimo Federici: Consultant for Novo Nordisk, Lilly and Amarin and Organon; speaker honoraria from Boehringer Ingelheim and Novo Nordisk. Manuel Romero-Gómez: Consultant for AbbVie, Alpha-sigma, Allergan, Astra Zeneca, Axcella Health, BMS, Boehringer Ingelheim, Echosens, Gilead, Intercept, Inventia, Kaleido, MSD, Novo Nordisk, Pfizer, ProSciento, Rubió, Siemens, Shionogi, Sobi and Zydus; research grants from Gilead, Intercept, Siemens, Theratechnologies, Echosens and Novo Nordisk. Jörn M. Schattenberg: Consultant for AstraZeneca, Apollo Endosurgery, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Gilead Sciences, GlaxoSmithKline, Intercept Pharmaceuticals, Ipsen, Inventiva Pharma, Madrigal, MSD, NorthSea Therapeutics, Novartis,

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Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.