



NASH Management Among Clinicians: Gaps in Clinical Competence and Practice Performance – Survey Findings

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Introduction

- Nonalcoholic steatohepatitis (NASH), the most serious form of nonalcoholic fatty liver disease (NAFLD), is characterized by steatosis, hepatocellular ballooning, lobular inflammation, and hepatic fibrosis, and can progress to cirrhosis, end-stage liver disease, and hepatocellular carcinoma (HCC).¹⁻³
- Since more than two thirds of adults in the United States are overweight/obese, a significant portion of the population is at risk of developing NASH, along with dyslipidemia and type 2 diabetes mellitus.^{3,4}
- Patients with NAFLD/NASH have a 9-fold increase in liver-related mortality, and are at increased risk of mortality from cardiovascular disease; NASH is also the third leading indication for liver transplantation.^{5,6}
- Since most patients with NASH are asymptomatic, many remain undiagnosed. A recent survey supporting this showed that patients are often underdiagnosed, even in academic settings.^{3,7}
- Currently, there is no approved pharmacologic therapy for the treatment of NASH, although a variety of agents are being explored in clinical trials.²
- Although primary care physicians are likely to be the first clinicians to encounter patients at risk for or with NASH, studies suggest that the majority do not consider NAFLD/NASH as a clinically important diagnosis; similarly, clinicians from other nonhepatology specialties state that NAFLD is uncommon in their practice.^{8,9}
- Another survey found gaps in implementing practice guidelines; while physicians may be aware of the guidelines for diagnosing and treating patients with NASH, they are not implementing them in clinical practice.¹⁰

- To assess the competence and practice performance of clinicians involved in the screening, diagnosis, and treatment of NASH, and to guide future educational programs, Projects In Knowledge, a continuing medical education (CME) provider certified by the Accreditation Council of CME (ACCME), conducted an online survey of hepatologists, gastroenterologists (GIs), internal medicine physicians (IMs), and family practice/primary care physicians (FP/PCPs) involved in the screening, diagnosis, and treatment of patients with NASH.

Methods

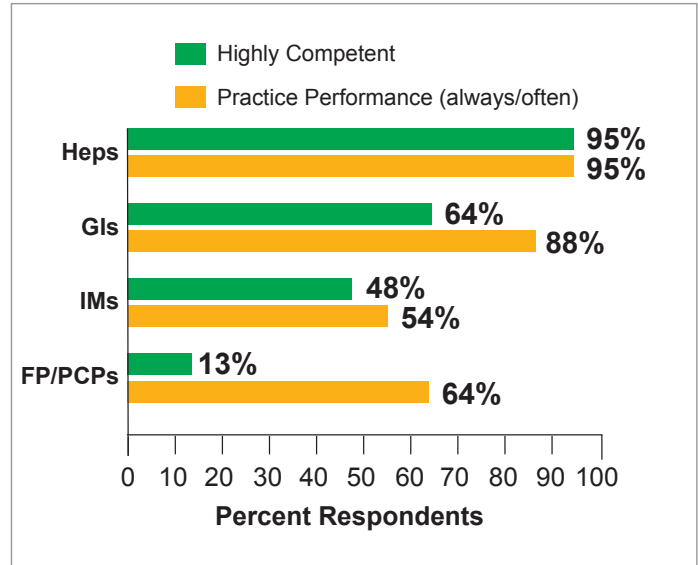
- Projects In Knowledge designed an online survey and emailed it to a proprietary database of 8510 clinicians, including hepatologists, GIs, IMs, and FP/PCPs.
- Clinicians surveyed were asked to self-assess whether they were highly, somewhat, or not at all competent with regard to specific NASH topics, such as risk factors/screening of at-risk patients; diagnosis; initiation of early treatment; criteria for treatment response; efficacy, safety, and adverse effect management of emerging NASH therapies; monitoring patients for response, adverse effects, and adherence; and the link between fatty liver, inflammation, cirrhosis, need for liver transplant, and mortality.
- Using a four-point scale ranging from always to never, they were also asked about the degree to which they perform interventions related to these topics in their practice (practice performance).
- Finally, the clinicians were asked to identify challenges and areas of educational needs in screening, diagnosing, and treating NASH.

Results

Of the 95 respondents to the Projects In Knowledge survey, 20 were hepatologists, 25 were GIs, 27 were IMs, and 23 were FP/PCPs.

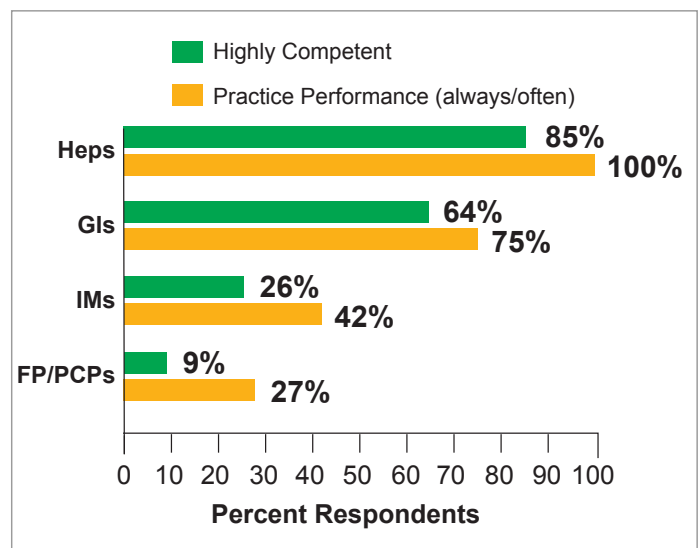
1 Risk Factors/Screen At-Risk Patients

- A high percentage of hepatologists state that they feel highly competent in screening at-risk patients (95%), and this is reflected in the percentage that always/often screen for NAFLD/NASH in at-risk patients in their practice (95%).
- However, physicians in other specialties report that, while they may screen patients, they do not have comparable confidence in their competence.
- This was particularly noticeable in the responses of GIs and FP/PCPs, who are in the front line for screening at-risk patients. Although 88% of GIs state that they always/often screen high-risk patients, only 64% feel highly competent in terms of risk factors and screening. 64% of FP/PCPs state that they always screen at-risk patients, but only 13% rate themselves as highly competent.



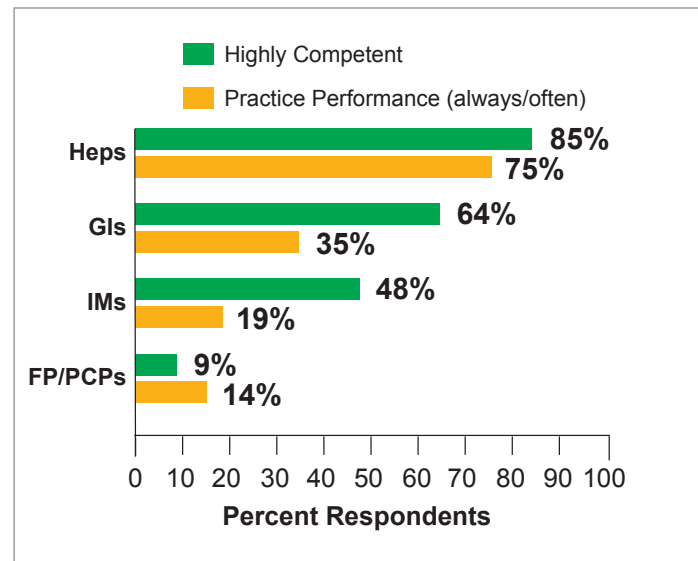
2 Diagnose NASH and Assess Prognosis

- Physicians in all four specialties report attempting to diagnose and assess prognosis despite not feeling highly competent to do so.
- 100% of the hepatologists state that they always/often diagnosis NASH and assess prognosis, yet only 85% feel highly competent in this.
- FP/PCPs report dramatically lower rates of practice performance and competence, with only 27% of FP/PCPs always/often diagnosing and assessing NASH patients and only 9% feeling highly competent in these areas.



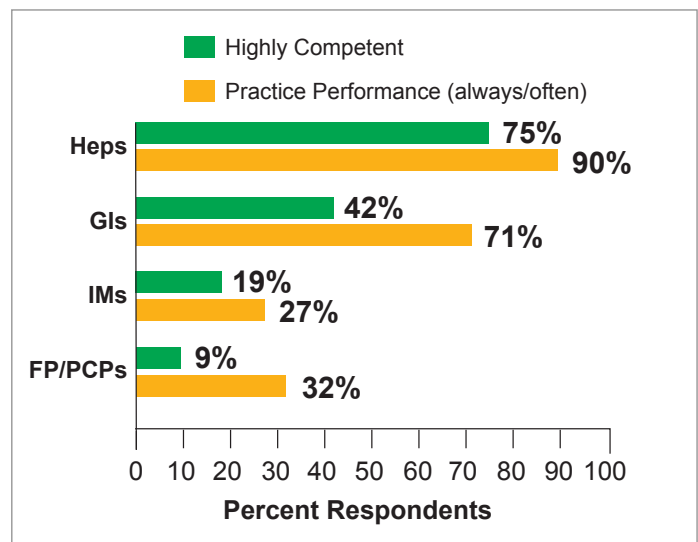
3 Importance of Early Diagnosis/Early Treatment or Trial Enrollment

- As hepatologists and GIs are the specialists most likely to treat patients with NASH, it's important to note the discrepancy between those who state they are highly competent in recognizing the importance of early diagnosis and treatment (85% and 64%, respectively) and those who actually initiate treatment or enroll patients in a clinical trial as soon as NASH is diagnosed (75% and 35%, respectively).
- IMs and especially FP/PCPs rarely initiate treatment or enroll patients in clinical trials upon diagnosis (19% and 14%, respectively).



4 Criteria/Endpoints to Assess Treatment Response

- Again, more hepatologists than other specialties report always/often utilizing endpoints in practice in assessing patient response to treatment (90%), but only 75% feel highly competent in terms of the criteria for response.
- GIs state that they utilize these endpoints in practice (71%), although they do not feel highly competent in doing so (42%).
- Similar gaps between practice performance (27% and 32%) and competence (19% and 9%) were noted for IMs and FP/PCPs, respectively.



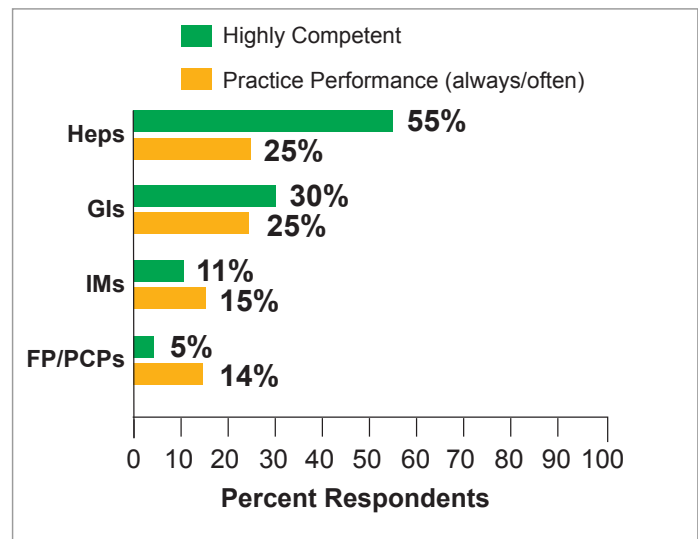
5 MOA, Efficacy, and Safety of Emerging NASH Treatments/Trial Enrollment

- Physicians in each of the four specialties report varying degrees of competence in discussing emerging NASH treatments, depending on the specific treatment in question.
- Hepatologists and GIs report feeling most competent in terms of discussing vitamin E, thiazolidinediones (TZDs), and pentoxifylline (65% and 33%, respectively).
- Less than 10% of IMs and FP/PCPs feel highly competent discussing emerging treatments.
- Hepatologists, GIs, and IMs are more likely to enroll their patients in trials with vitamin E, TZDs, and pentoxifylline than with other investigational agents (40%, 38%, and 15%, respectively), while FP/PCPs, are slightly more likely to enroll patients in trials with Px102/Px104 (20%).

Treatment	Hepatologists		GIs		IMs		FP/PCPs	
	Competence	Practice Performance	Competence	Practice Performance	Competence	Practice Performance	Competence	Practice Performance
Vitamin E, TZDs, pentoxifylline	65%	40%	33%	38%	7%	15%	5%	14%
Obeticholic acid	45%	32%	16%	25%	7%	12%	5%	14%
Px102/Px104	25%	35%	16%	21%	0%	8%	5%	20%
Simtuzumab	25%	25%	13%	17%	4%	12%	4%	10%
GFT-505	30%	25%	9%	21%	0%	4%	5%	14%
Cenicriviroc	20%	25%	8%	21%	4%	8%	9%	15%
Aramchol	20%	25%	9%	21%	4%	4%	5%	5%

6 Monitoring Treatment Response Endpoints, Adverse Effects, and Adherence

- Only 25% of the hepatologists and of the GIs surveyed state that they always/often monitor their patients for response, adverse effects, and adherence, although 55% and 30%, respectively, rate themselves as highly competent in monitoring endpoints in these areas.



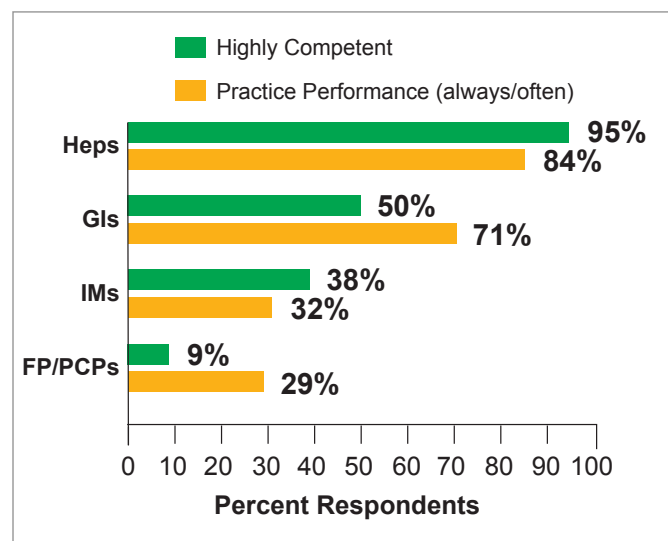
7 Assess/Manage Treatment-Related Adverse Effects of Emerging Treatments

- The percentage of physicians who assess and manage adverse effects of emerging treatments varies from 0% to 55% depending on the specialty and the treatment in question.
- Particularly notable is the fact that less than 10% of IMs and FP/PCPs see themselves as highly competent in managing treatment-related adverse effects associated with any of these emerging therapies, compared with up to 75% of hepatologists and up to 38% of GIs.

Treatment	Hepatologists		GIs		IMs		FP/PCPs	
	Competence	Practice Performance	Competence	Practice Performance	Competence	Practice Performance	Competence	Practice Performance
Vitamin E, TZDs, pentoxifylline	75%	55%	38%	50%	8%	15%	9%	20%
Obeticholic acid	40%	35%	17%	21%	4%	12%	9%	14%
Px102/Px104	25%	25%	8%	21%	0%	8%	5%	0%
Simtuzumab	25%	25%	13%	21%	4%	12%	5%	19%
GFT-505	20%	25%	8%	17%	0%	4%	5%	10%
Cenicriviroc	20%	30%	8%	21%	4%	8%	5%	14%
Aramchol	15%	25%	8%	21%	0%	8%	5%	14%

8 Link Between Fatty Liver, Inflammation, Fibrosis, Cirrhosis, HCC, Need for Liver Transplantation, and Mortality/Monitoring for These Conditions

- 95% of hepatologists rate themselves as highly competent in understanding the link between these conditions and mortality, yet a smaller percentage (84%) monitor inflammation, fibrosis, cirrhosis, HCC, change in NASH status.
- In contrast, more GIs always/often monitor their patients for these conditions (71%) than feel highly competent in understanding the link between these conditions and mortality (50%).



9 Challenges and Educational Needs

- Clinicians in all four specialties express a desire for education regarding diagnosis, adherence to treatment, and updates on emerging NASH therapies.
- Other areas of particular interest include state-of-the-science regarding NASH and how to enroll patients in clinical trials in their area.

Challenges/Education Needed to Manage and Treat NASH Patients	Hepatologists (n = 20)	GIs (n = 25)	IMs (n = 27)	FP/PCPs (n = 23)
Screening for NASH				✓
NASH guidelines		✓	✓	
Strategies to diagnose fibrosis; when do liver biopsy	✓	✓	✓	✓
Risk stratification			✓	
How to evaluate disease progression		✓		
Adherence to treatment	✓	✓	✓	✓
Update on state-of-the-science of NASH		✓	✓	✓
No FDA-approved NASH therapies	✓	✓	✓	✓
Updates needed on emerging NASH therapies and management strategies	✓	✓	✓	✓
How to enroll patients in clinical trials within area	✓	✓	✓	

Conclusions

- Substantial gaps between clinical competence and practice performance were identified in virtually all the areas discussed, with overall need for education in diagnostic testing (including when/when not to do a liver biopsy), endpoints for treatment response, NASH updates, emerging treatments and their efficacy and adverse effect management, and how to enroll patients in clinical trials.
- As would be expected, hepatologists demonstrated a higher level of competence and practice performance relative to other specialties but gaps were seen even in this group.
- Only 64% and 42% of GIs feel highly competent in screening and criteria/endpoints for treatment response, respectively, yet 88% and 71% state that they always/often screen patients and utilize endpoints for treatment response, respectively; thus, many GIs are performing actions in their practice for which they do not feel highly competent.
- Given that hepatologists and gastroenterologists are presumably the most competent in the care of NASH patients, gaps in their competence and practice performance have important implications for the quality of patient care.
- Very few FP/PCPs (4%–13%) and IMs (48% or less) feel highly competent in any of the areas discussed. Since these are the clinicians involved in front-line screening and referral, these gaps in competence and practice performance have important healthcare implications.
- Focusing education on the specific needs of different specialties can inform and provide improved practice performance.

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Disclosures

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