2020

Liver Health

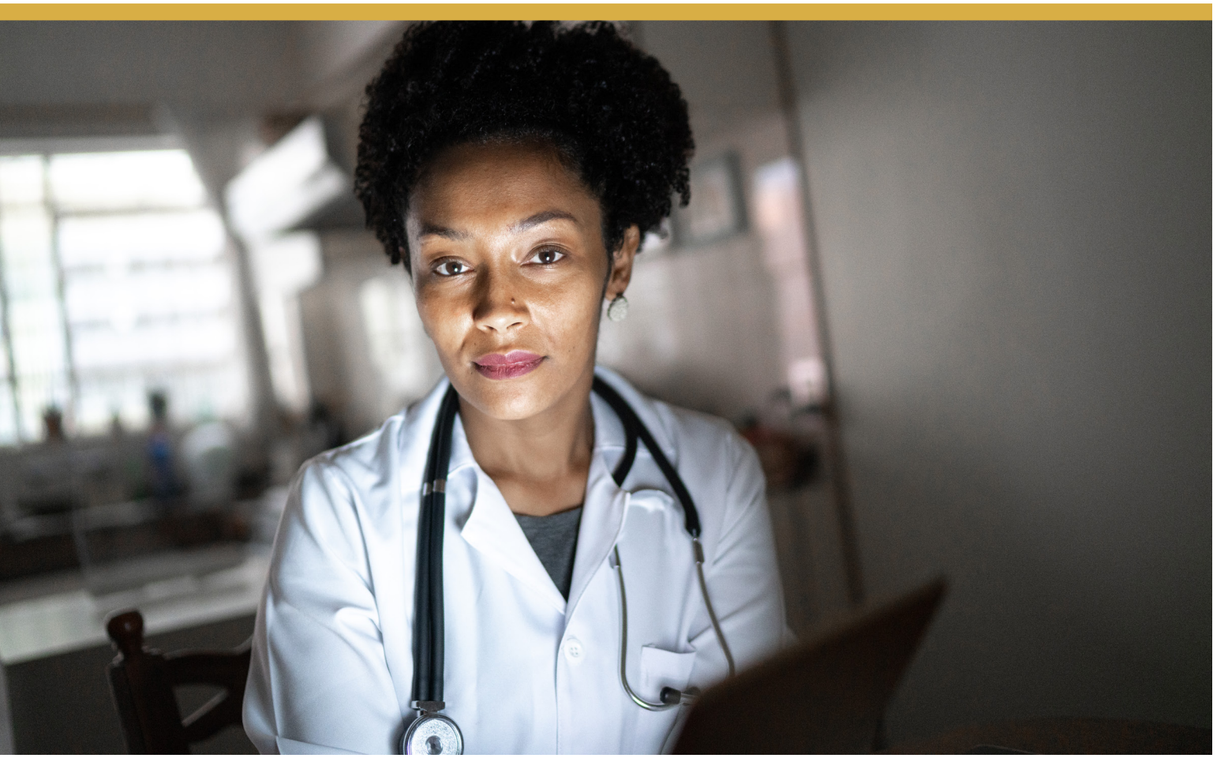
Annual Trends Report

Third Edition

FACING THE COMPLEXITY
of Chronic Liver Disease

Salix Pharmaceuticals

LIVERHEALTHNOW™



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Foreword

On behalf of Salix, I would like to thank the panel of experts, survey respondents, interview participants, and contributors for their diligent work and valuable insights into the current state of liver health in the United States. This report provides an updated overview of the trends and challenges facing patients with chronic liver disease (CLD), especially those with nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH). NAFLD is one of the most common causes of liver disease in the United States.[1] The report also highlights the disparities and gaps in care that affect different populations and regions, as well as the opportunities and strategies to improve the quality and outcomes of CLD and cirrhosis management.

The findings detailed in this report are alarming and call for urgent action from all stakeholders involved in liver health, including policymakers, health care providers, researchers, patients, and advocates. CLD and cirrhosis mortality increased by 9% in 2021 from 2020, making them the ninth leading cause of death in the United States.[2] This increase is largely driven by the rising prevalence of NAFLD and NASH, which are associated with obesity and diabetes.[3] The report also reveals that NAFLD affects 1 in 4 Hispanics, making them the most affected ethnic group in the United States.[4] Moreover, the report indicates that there is a shortage of liver specialists—especially in rural areas—that is impacting care. Rural primary care providers who are filling this gap in care need more education, support, and practical guidelines to effectively diagnose and manage CLD and cirrhosis patients.

As a sponsor of this report, Salix is committed to supporting the efforts to address these challenges and to educate around better liver health in the United States as part of an initiative we are calling the "Groundswell" campaign. Groundswell is our way of describing grass-root action by all CLD stakeholders to raise awareness and promote improved CLD patient care. We hope that this report will serve as a useful resource and a catalyst for action for all those who care about improving liver health. Please join us in this "Groundswell" effort—we can make a difference in the lives of millions of Americans living with CLD.

To access a PDF version of this report, a companion presentation, and other educational resources, go to **liverhealthnow.com/trends-report**.

Nicola Kayel
Senior Vice President, Salix Marketing
Salix Pharmaceuticals

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Introduction

Clinical Perspective

Salix Pharmaceutical's third edition of the *Liver Health Annual Trends Report* presents valuable data and clinician insights concerning the growing issue of chronic liver disease (CLD). As the ninth leading cause of death in the United States, CLD is a significant public health concern that suffers from a lack of awareness.[5] This year's report emphasizes the need for improvements in care and clinician education.

While we were working on this edition of the *Trends Report*, the American Association for the Study of Liver Diseases (AASLD) shared that new fatty liver disease nomenclature was announced in June 2023.[6] (See box below.) Since the nomenclature is so new, we made the decision to use the old nomenclature in the text to avoid confusion.

The report reveals important findings, including a significant increase in patients with nonalcoholic fatty liver disease (NAFLD) and alcohol-associated liver disease (ALD), which has been reported during the COVID pandemic.[7,8] As these numbers rise, gastroenterologists report a 32% increase in CLD patients and a 54% increase in patients with cirrhosis per month.

The primary research identifies socioeconomic factors and staffing shortages as contributing to the challenge of providing adequate care, especially in rural and underserved areas. Patients wait an average of 13.1 weeks to establish care with a specialist, but in some rural areas, the wait time can extend to just under a year.

Our patients count on us to provide them with the best care possible. With the rise in cases of NAFLD and ALD, it's more important than ever to stay informed so we can help our patients manage their conditions. By leveraging the right resources, we can make a significant impact on their health and well-being, minimizing complications like cirrhosis and hepatic encephalopathy. The *Liver Health Annual Trends Report* enables us to equip ourselves with the knowledge and tools needed to provide our patients with the care, guidance, and support they need to achieve better outcomes.

Nancy Reau, MD
Rush University Medical Center

New Fatty Liver Disease Nomenclature Announced in June 2023[6]

- **Steatotic liver disease (SLD)**—overarching term to encompass the various etiologies of steatosis
- **Metabolic dysfunction–associated steatotic liver disease (MASLD)**—formerly nonalcoholic fatty liver disease (NAFLD); encompasses patients who have hepatic steatosis and have at least 1 of 5 cardiometabolic risk factors
- **Metabolic alcohol-associated liver disease (MetALD)**—those with MASLD who consume greater amounts of alcohol per week (140 g to 350 g/week and 210 g to 420 g/week for females and males, respectively)
- **Cryptogenic SLD**—those with no metabolic parameters and no known cause
- **Metabolic dysfunction–associated steatohepatitis (MASH)**—formerly nonalcoholic steatohepatitis (NASH)

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Patient Advocacy Perspective

This research on patient perspectives on stigma around liver disease bolsters the strong foundation of this third edition of the *Liver Health Annual Trends Report*. By quantifying and identifying key themes of the patient experience with chronic liver disease (CLD), this *Trends Report* creates a roadmap for each of the players in the field to reduce stigma for all liver patients moving forward.

The findings underscore concerns liver patients have engaged for years—that patients need timely, comprehensive education and awareness of disease risks, stages, progression, and treatment options; that non-stigmatizing, best-practice screening should be universally adopted; and that patients' lived experience and humanity must be recognized. It is heartening to see patients' lived experiences formalized and tied to concrete solutions. I am encouraged to find the priorities identified are those that the Global Liver Institute successfully addresses through our programming, education, and advocacy.

This research reinforces the need for patient advocacy and involvement to develop policies that reduce and eliminate stigma rather than perpetuate it. Let us not allow formality to distract from the fact that empathy is central to every piece of the solution—including policy measures at national, local, and health system levels.

Thank you to Salix Pharmaceuticals for this critical research and review. As you read, I encourage you to examine what stigma you may harbor around CLD and consider actions you can take to reduce structural and public stigma for CLD patients around the world.

Donna R. Cryer, JD
Chief Executive Officer
Global Liver Institute

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Key Findings

New Fatty Liver Disease Nomenclature Announced in June 2023[6]

- **Steatotic liver disease (SLD)**—overarching term to encompass the various etiologies of steatosis
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- **Cryptogenic SLD**—those with no metabolic parameters and no known cause
- **Metabolic dysfunction–associated steatohepatitis (MASH)**—formerly nonalcoholic steatohepatitis (NASH)

This third edition of the *Liver Health Annual Trends Report* continues to document the landscape of chronic liver disease (CLD) and cirrhosis in the United States as well as trends impacting quality and disparities of care. Increased mortality is being driven by increases in the prevalence of alcohol- and non–alcohol-related CLD and cirrhosis likely due to obesity, diabetes, and COVID-19 and compounded by socioeconomic challenges and disparities in CLD patient management, particularly shortages of liver specialists. The nonalcoholic fatty liver disease (NAFLD) burden is the highest and fastest growing among Hispanics, with an estimated prevalence of 1 in 4. Research in this report indicates that primary care physicians (PCPs), nurse practitioners (NPs), and physician assistants (PAs) are helping address this gap in care, particularly in rural settings; however, they need education, electronic health record (EHR) resource support, and guidelines that are more easily translatable to their daily practice.

SECONDARY RESEARCH FROM PEER-REVIEWED PUBLICATIONS

In 2021, increased deaths due to CLD and cirrhosis of 9% resulted in them becoming the ninth leading cause of death in the United States.[2]

A contributing factor to the increase in CLD and cirrhosis mortality is being driven by the growing prevalence of NAFLD and nonalcoholic steatohepatitis (NASH), currently estimated at 25% and 5% respectively of the US population, with mortality anticipated to nearly triple by 2030.[3,9,10]

There are significant racial and ethnic disparities in the NAFLD population. The NAFLD burden is the highest and fastest growing among Hispanics, with an estimated prevalence of 1 in 4.[4]

PRIMARY MARKET RESEARCH

Gastroenterologists are seeing statistically significant more patients per month versus last year (eg, 91 patients with CLD per month [+32%] and 54 patients with cirrhosis per month [+54%]). **[Figure 2]**

In the last calendar year, as compared to pre-pandemic levels, 41% of gastroenterologists saw an increase in NAFLD, 38% reported increases in NASH, and 33% of gastroenterologists saw an increase in alcohol-associated liver disease. Similar increases were reported by NPs/PAs. **[Figure 4]**

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In the last calendar year, as compared to pre-pandemic levels, 32% of gastroenterologists report observing increases in the number of patients presenting with elevated liver enzymes, 28% report seeing an increase in hospitalizations due to alcoholic cirrhosis, and 20% report seeing increases in younger patients requiring liver transplantation. NPs/PAs saw a 49% increase in elevated liver enzymes versus pre-pandemic levels. **[Figure 5]**

A key area of exploration this year was to better understand the disparities in care in the treatment and management of liver disease. Key factors leading to disparities in care for liver disease patients include the following:

- This year, all socioeconomic factors impacting liver disease patient outcomes experienced statistically significant increases in their importance ratings (at 95% confidence). For example, food security rose 53%. **[Figure 6]**
- Overall, 72% of all respondents report that their organizations have suffered chronic staffing shortages across many roles. Eighty percent of respondents reported chronic nursing shortages within their organizations. A lesser 29% report shortages of gastroenterologists, and 26% report shortages of hepatologists. Respondents report that shortages in hepatologists and gastroenterologists have the greatest impact on their organization's ability to manage liver disease patient care (82% and 77%, respectively). **[Figure 7]**
- While disparities of care can and do happen in all parts of the country, several issues were amplified in the survey results of those providers working in rural locations. For example, for providers working in rural locations, the average wait time for a patient to see a liver disease specialist is 13.1 weeks, with a standard deviation (SD) of 29.7 (indicating a wide range [eg, wait times almost 1 year]) compared with 7.6 weeks (SD 6.5) for urban/suburban locations. **[Figure 9]**

With respect to practice management and resources:

Thirty-one percent of surveyed respondents who treat liver disease are unaware of any national guidelines for the management of CLD. **[Figure 15]**

There were no significant changes in awareness of guidelines except among PCPs, who reported a statistically significant increase in awareness for cirrhosis guidelines, an increase of 27% versus last year (51% to 65%). **[Figure 15]**

Sixty-eight percent of respondents reported that it is important/very important to align their CLD treatment management with national treatment guidelines, a statistically significant increase of 13% versus last year. **[Figure 16]**

Of those who said they utilize national guidelines for liver disease care management (N=320), 56% of respondents say they are interested in these guidelines but not sure how to translate the information into daily practice, a statistically significant increase of 332% versus last year. **[Figure 17]**

There was a statistically significant increase of 34% in the importance of the use of third-party guidelines versus 2022 (44% to 59%). **[Figure 13]**

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Respondents had statistically significant increases in their importance ratings versus last year for several of their liver disease resources: **[Figure 36]**

+34% Guidelines created by third parties

+72% Liver disease information and resources in the EHR

+40% Liver disease order set or pathway in the EHR system

Methodology

This trends report on chronic liver disease (CLD) includes information collected from an online survey, qualitative telephone interviews, and secondary research from peer-reviewed publications. An independent third-party recruiting firm invited over 400 health care providers to participate in this research during April and May of 2023. Provider participation (N=400) sought national representation and was comprised of the following subgroups: 100 gastroenterologists, 100 hospital-based specialists, 100 primary care physicians (PCPs), and 100 nurse practitioners/physician assistants (NPs/PAs). Follow-up telephone interviews were conducted with N=20 providers (Table 1). Quotes from the in-depth interviews throughout this report represent the opinions of those respondents. Respondents self-reported on their place of work as being either an urban, suburban, or rural location; and a subgroup analysis was completed to compare findings from respondents. In the urban/suburban group, there were N=356 survey respondents, comprised of the following subgroups: 98 gastroenterologists, 92 hospital-based specialists, 87 PCPs, and 79 NPs/PAs. The rural subgroup was significantly smaller (N=44) and was comprised of 2 gastroenterologists, 8 hospital-based specialists, 13 PCPs, and 21 NPs/PAs.

Limitations of Market Research and Statistical Analysis

Readers should be aware that the market research and statistical analysis in this report were conducted in a manner consistent with industry standards and market research codes of conduct. Market research of this type is based on a random sample and reports on aggregated respondents' perceptions. This is in no way comparable to the scientific rigor of clinical research. As it pertains to the online survey, analysis was conducted utilizing the QPSMR data analysis software; all statistical significance in this report is at 95% confidence.

Several survey questions utilize a Likert scale and top 2 box score reporting methodology. In these questions, respondents are asked to select a response on a 7-point scale that best matches the respondent's perception (eg, on a scale of 1 to 7, where 1 is not important and 7 is very important). The top 2 box score refers to the percentage of respondents that select a 6 or 7 response from the Likert scale (eg, "important/very important").

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Secondary research was conducted utilizing Google and PubMed searches to identify relevant peer-reviewed publications and sources as noted in the report. Furthermore, treatment utilization and claims data were sourced from IQVIA. Secondary research may not reflect all published data. A systematic review was not performed.

Table 1 | **Participant Demographics**

Online Survey, N=400									
		Gastroenterologists N=100		**Hospital-based Specialists** N=100		**Primary Care Physicians** N=100		**NPs/PAs** N=100 (50 NPs, 50 PAs)	
		2023	2022	**2023**	2022	**2023**	2022	**2023**	2022
Geographic Location	Northeast	**30%**	36%	**18%**	13%	**13%**	24%	**18%**	17%
	Midwest	**19%**	20%	**15%**	19%	**22%**	24%	**20%**	27%
	South	**36%**	23%	**40%**	36%	**41%**	27%	**42%**	33%
	West	**15%**	21%	**27%**	32%	**24%**	25%	**20%**	23%
Practice Type	Urban	**40%**	N/A	**43%**	N/A	**35%**	N/A	**38%**	N/A
	Suburban	**58%**	N/A	**49%**	N/A	**52%**	N/A	**41%**	N/A
	Rural	**2%**	N/A	**8%**	N/A	**13%**	N/A	**21%**	N/A
In-depth Telephone Interviews N=20		**8 (40%)**	5 (25%)	**2 (10%)**	7 (35%)	**6 (30%)**	4 (20%)	**4 (20%)**	4 (20%)

Area of Specialization	**Hospital-based Specialists**			**NPs/PAs**		
	ER Physicians	**35%**	26%	Internal Medicine	**18%**	17%
	Internists	**35%**	35%	Gastroenterology	**20%**	27%
	Hospitalists	**25%**	31%	Family Medicine	**42%**	33%
	Hepatologists	**5%**	8%	Other	**20%**	23%

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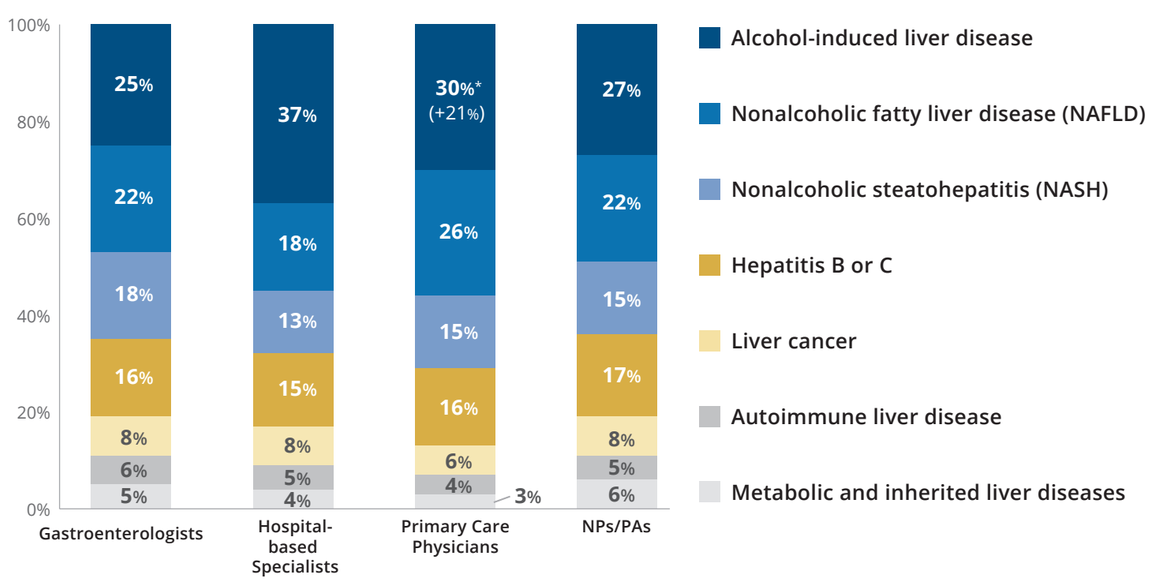
An expert panel was convened at commencement of the project to provide guidance on the development of the third edition, including feedback on the previous edition. The expert panel also reviewed a final draft of the third edition of the report and provided verbatims and observations on the findings, some of which have been included. Expert panel participants were:

- **James Hanje, MD, FAASLD**: Co-Medical Director, OGGI/Ohio Health Comprehensive Liver Center, Columbus, OH
- **Edward A. Mena, MD**: Director of Hepatology for HealthCare Partners medical group, Lead Physician at the Temple City Site, involved on the transplant committee for HealthCare Partners
- **Nancy Reau, MD**: Professor of Medicine at Rush University Medical Center, Richard B. Capps Chair of Hepatology, Chief, Section of Hepatology, Associate Director, Solid Organ Transplantation
- **Sammy Saab, MD, MPH**: Professor in the Departments of Medicine and Surgery at the David Geffen School of Medicine at UCLA, Medical Director of the UCLA Adult Liver Transplant Program, and the Chief of Transplant Hepatology

Figure 1 | **Types of Liver Disease Participants Treat**

Q2. What percentage of the chronic liver disease patient population that you treat have the following conditions (total must equal 100%)?



N=400 (100 Gastroenterologists, 100 Hospital-based Specialists, 100 PCPs, 100 NP/PAs).
*This number is statistically significant at 95% confidence versus last year.
Values in parentheses indicate percent change from 2022.

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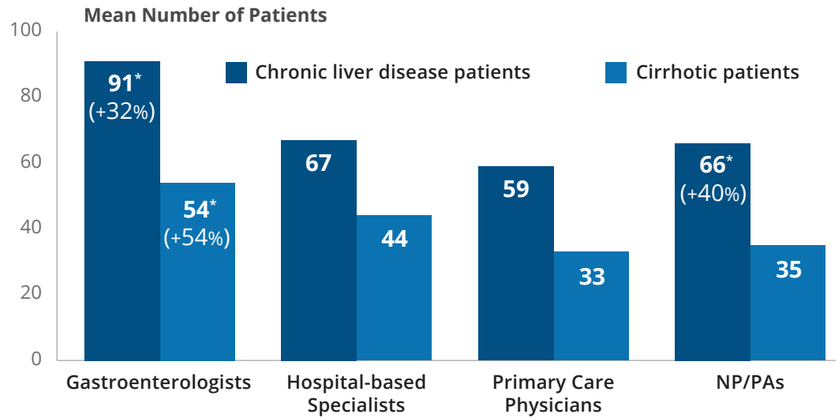
Figure 2 | **Average Number of Liver Disease Patients Seen Monthly**

SQF. On average, how many chronic liver disease and cirrhotic patients do you personally see/treat in a typical month?



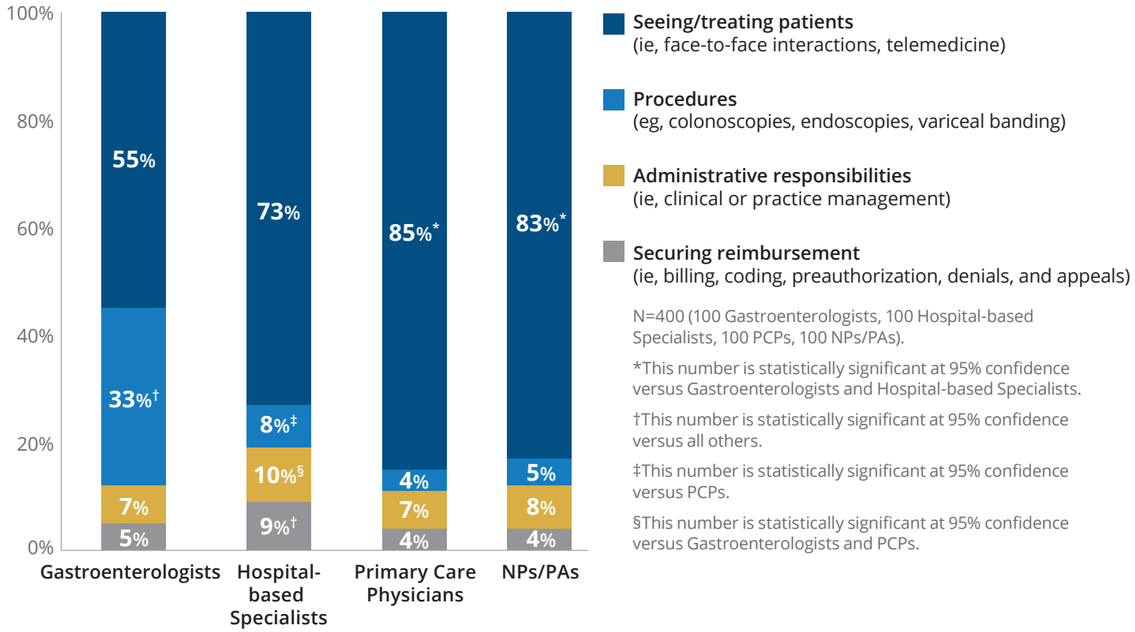
N=400 (100 Gastroenterologists, 100 Hospital-based Specialists, 100 PCPs, 100 NPs/PAs).
*This number is statistically significant at 95% confidence versus last year.
Values in parentheses indicate percent change from 2022.

Figure 3 captures the time respondents spend in an average week doing work-related tasks.

Respondents located in urban and suburban areas spend twice as much time securing reimbursement versus rural providers (6% versus 3%).

Figure 3 | **Respondent Time Spent Doing Work-related Tasks**

Q3.21. In an average week, how much time do you spend doing the following activities?



N=400 (100 Gastroenterologists, 100 Hospital-based Specialists, 100 PCPs, 100 NPs/PAs).
*This number is statistically significant at 95% confidence versus Gastroenterologists and Hospital-based Specialists.
†This number is statistically significant at 95% confidence versus all others.
‡This number is statistically significant at 95% confidence versus PCPs.
§This number is statistically significant at 95% confidence versus Gastroenterologists and PCPs.

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Burden of Illness

Key Findings:

SECONDARY RESEARCH FROM PEER-REVIEWED PUBLICATIONS

In 2021, a 9% increase in deaths due to chronic liver disease (CLD) and cirrhosis resulted in them becoming the ninth leading cause of death in the United States.[2]

A contributing factor to the increase in CLD and cirrhosis mortality is being driven by the growing prevalence of NAFLD and nonalcoholic steatohepatitis (NASH), currently estimated at 25% and 5% respectively of the US population, with mortality anticipated to nearly triple by 2030.[3,9,10]

There are significant racial and ethnic disparities in the NAFLD population. The NAFLD burden is the highest among Hispanics, with an estimated prevalence of 1 in 4.[4]

The COVID-19 pandemic exacerbated poorer outcomes, including an increase in alcohol-associated liver disease (ALD) deaths of 22.4% (2020 versus 2019; and for the first time, ALD accounted for more liver transplant wait-listings (40.1%) than hepatitis C virus (12.4%) and NASH (23.4%) combined.[7,11]

PRIMARY MARKET RESEARCH

Gastroenterologists are seeing statistically significant more patients per month versus last year (eg, 91 patients with CLD per month [+32%] and 54 patients with cirrhosis per month [+54%]). **[Figure 2]**

In the last calendar year, as compared to pre-pandemic levels, 41% of gastroenterologists saw an increase in NAFLD, 38% reported increases in NASH, and 33% of gastroenterologists saw an increase in ALD. Similar increases were reported by nurse practitioners/physician assistants (NPs/PAs). **[Figure 4]**

In the last calendar year, as compared to pre-pandemic levels, 32% of gastroenterologists report observing increases in the number of patients presenting with elevated liver enzymes, 28% report seeing an increase in hospitalizations due to alcoholic cirrhosis, and 20% report seeing increases in younger patients requiring liver transplantation. NPs/PAs saw a 49% increase in elevated liver enzymes versus pre-pandemic levels. **[Figure 5]**

Please see the Methodology (page 10 of this report) Limitations of Market Research and Statistical Analysis section.

New Fatty Liver Disease Nomenclature Announced in June 2023[6]

- **Steatotic liver disease (SLD)**—overarching term to encompass the various etiologies of steatosis
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SECONDARY RESEARCH FROM PEER-REVIEWED PUBLICATIONS

The Clinical and Economic Burden of Chronic Liver Disease

Chronic liver disease and cirrhosis became the ninth leading cause of death in 2021.[2]

In 2021, there were 14.5 age adjusted CLD and cirrhosis deaths per 100,000 US population compared with 13.3 per 100,000 in 2020—approximately a 9% increase.[2]

According to a cross-sectional study of hospitalized adults with CLD in the United States (n=1,016,743) using data from the National Inpatient Sample from 2012-2016, during that time period[12]:

- Annual hospitalization rates (per 100,000) increased by 20.8%.
- Mean hospitalization costs for CLD patients increased 26.2%.
- In 2016, Asian/Pacific Islanders had a higher total in-hospital mortality rate (8.3%), followed by African Americans (7.7%), Whites (7.3%), and Hispanics (6.0%).

The Impact of NAFLD and NASH

NAFLD affects approximately 25% of the US population. Most patients with NAFLD are undiagnosed.[13]

Barriers to the diagnosis of NAFLD include[14]:

- Asymptomatic nature of the condition
- Lack of standardized diagnostic tools
- Lack of awareness among both patients and professionals.

Prevalence of NAFLD and NASH is projected to increase 21% and 63%, respectively, between 2015 and 2030 due to high rates of diabetes and obesity.[3]

Mortality from liver disease associated with NAFLD progression is projected to nearly triple by 2030.[3]

Initial evaluation of patients with suspected NAFLD should carefully consider the presence of commonly associated comorbidities such as obesity, dyslipidemia, insulin resistance or diabetes, hypothyroidism, polycystic ovary syndrome, and sleep apnea.[13]

NASH is a form of NAFLD in which there is inflammation of the liver and liver damage, in addition to fat in the liver. NASH may lead to cirrhosis.[9] About 5% of US adults have NASH.[10] Both NAFLD and NASH are contributors to and markers for increased cardiovascular disease risk.[14]

Note: The market research and statistical analysis in this report were conducted in a manner consistent with industry standards and market research codes of conduct; however, this is in no way comparable to the scientific rigor of clinical research. All statistical significance in this report is at 95% confidence.

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Racial and Ethnic Disparities in NAFLD Prevalence

A systematic review and meta-analysis of 34 studies up to August 2016, with a total of 368,569 patients, revealed the following information.[4]

Pooled relative risk of NAFLD among hospitalized patients[4]:

- Hispanics: relative risk of 1.47 (95% confidence interval [CI]: 1.35-1.61) compared with whites
- Blacks: relative risk of 0.74 (95% CI: 0.69-0.80) compared with whites

NAFLD prevalence[4]:

- Hispanics: 22.9% (95% CI: 21.6%-24.1%)
- Whites: 14.4% (95% CI: 14.0%-14.8%)
- Blacks: 13% (95% CI: 12.2%-13.9%)

NASH prevalence[4]:

- Hispanics: 45.4% (95% CI: 40.7%-50.2%)
- Whites: 32.2% (95% CI: 30.7%-33.7%)
- Blacks: 20.3% (95% CI: 16.8%-24.2%)

The highest NAFLD burden was among Hispanics, the fastest-growing demographic in the United States. Population-based studies suggest nearly 1 in 4 Hispanics have NAFLD compared with approximately 1 in 10 blacks.[4]

COVID-19 Severity and Mortality Among Chronic Liver Disease Patients

A meta-analysis of 40 retrospective studies totaling 908,032 participants indicated that CLD is associated with increased adverse clinical outcomes in terms of severity of disease and death among COVID-19 patients.[15]

- The odds of developing severe disease among COVID-19 patients with CLD were 2.44 times higher than among those without CLD.[15]
  - Subgroup analysis showed that COVID-19 patients with NAFLD had the highest odds of COVID-19 severity (pooled odds ratio [OR]=5.60; 95% CI: 1.52-20.64), followed by metabolic-associated fatty liver disease (MAFLD) (pooled OR=3.20; 95% CI: 1.99-5.14) and cirrhosis (pooled OR=3.09; 95% CI: 1.95-4.89).[15]
- COVID-19 patients with CLD had 2.35 times higher odds of dying as patients without CLD.[15]
- COVID-19 patients with cirrhosis had 3.51 times higher odds of dying as patients without cirrhosis (pooled OR=3.51; 95% CI, 2.41-5.10).[15]

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Preexisting Liver Disease Outcomes in Patients With COVID-19

- In a study of 2780 patients with COVID-19 (including 250 patients with CLD), patients with CLD had higher rates of mortality compared with those without liver disease after propensity score matching (12% versus 4%; risk ratio [RR]: 3.0; 95% CI: 1.5-6.0; P=0.001); and the relative risk was even higher in patients with cirrhosis.[8]
- Patients with preexisting liver disease also had a higher hospitalization rate following propensity score matching compared with those without liver disease (48% versus 36%; risk ratio: 1.3; 95% CI: 1.1-1.6).[8]
- Among patients with chronic liver disease, NAFLD and NASH (42%) were the most common etiologies.[8]

Incidence of Alcohol-related Liver Disease During the Pandemic

Death certificates from the National Center for Health Statistics were used to assess changes in alcohol-related deaths during the first year of the COVID-19 pandemic. Deaths involving alcohol jumped 25.5% between 2019 to 2020, totaling 99,107 deaths overall.[11]

The study showed that alcohol-associated liver disease deaths increased 22.4% (from 24,106 to 29,504) with the largest change occurring among people ages 55-64 (13.4%).[11]

Reasons for the unprecedented increase in alcohol-related deaths during the first year of the pandemic are still being explored. In 2020, the first year of the pandemic, consumption of alcohol increased by 2.9%, the largest annual increase in over 50 years.[16]

For the first time alcohol-associated liver disease (ALD) accounted for more liver transplant listings (40.1%) than hepatitis C virus (12.4%) and NASH (23.4%) combined. In addition, the severity of liver disease at time of listing and transplantation was also higher in patients with ALD.[7]

PRIMARY MARKET RESEARCH

Figure 4 captures respondents' observations of changes in the incidence of their liver disease patient populations (increased/significantly increased) in the last calendar year versus pre-pandemic times.

"In general, we are definitely seeing more patients than before the pandemic—a lot more acute alcoholic liver disease as well as chronic. We are seeing patients who probably should've seen us 2-3 years ago. The other explosion is NASH."

—Gastroenterologist

In the last calendar year, as compared to pre-pandemic levels, 41% of gastroenterologists saw an increase in NAFLD, 38% reported increases in NASH, and 33% of gastroenterologists saw an increase in ALD. Similar increases were reported by NPs/PAs.

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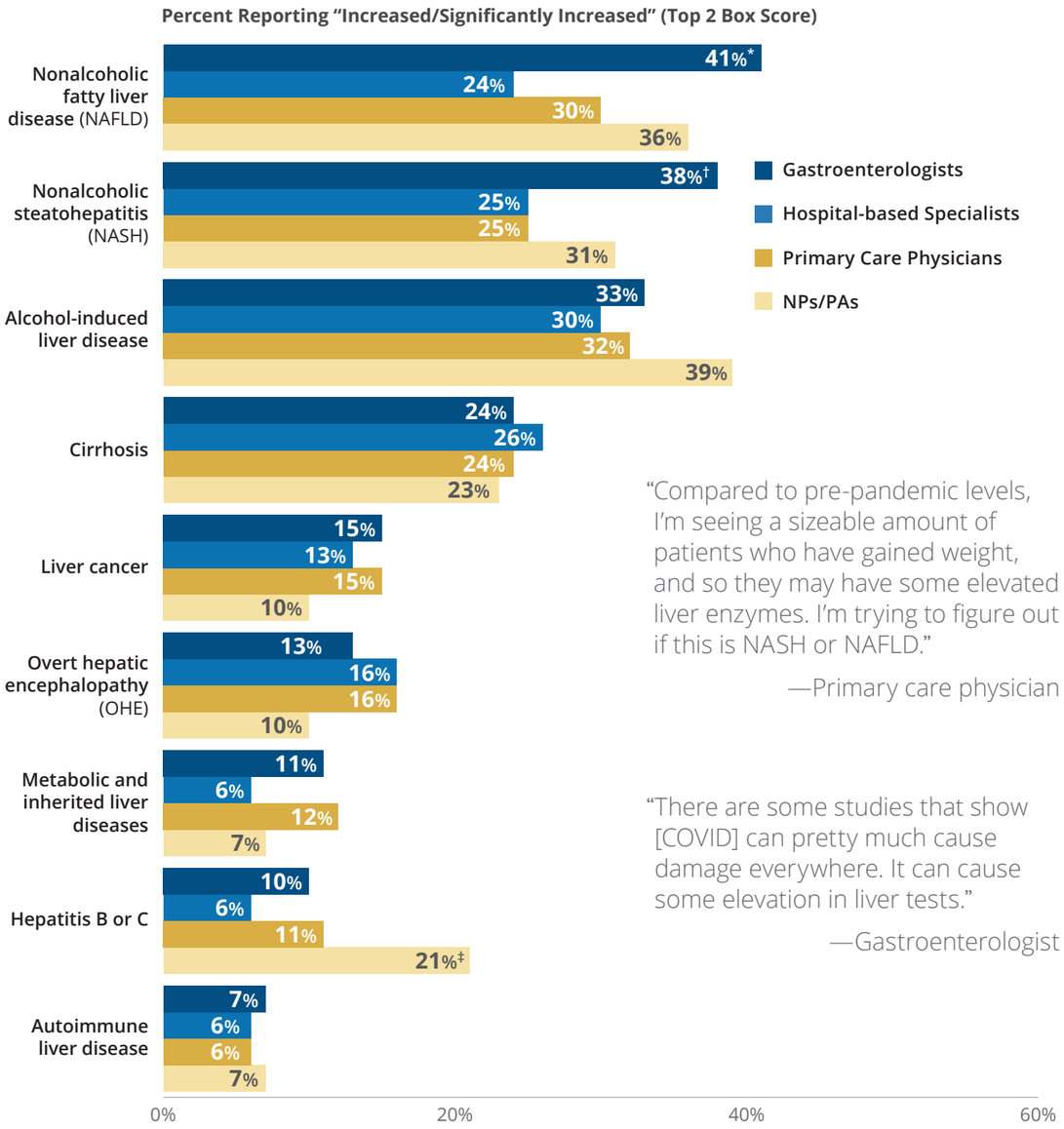
Figure 4 | **Changes Observed in Liver Disease Incidence Versus Pre-pandemic Levels**

Q3.24. Please indicate any changes in the incidence of the following types of liver disease patients that you or your institution experienced in the last calendar year as compared to 3 years ago (pre-pandemic). Please use a 7-point scale, where 1=significantly decreased and 7=significantly increased.



"Compared to pre-pandemic levels, I'm seeing a sizeable amount of patients who have gained weight, and so they may have some elevated liver enzymes. I'm trying to figure out if this is NASH or NAFLD."

—Primary care physician

"There are some studies that show [COVID] can pretty much cause damage everywhere. It can cause some elevation in liver tests."

—Gastroenterologist

N=400 (100 Gastroenterologists, 100 Hospital-based Specialists, 100 PCPs, 100 NPs/PAs).
*This number is statistically significant at 95% confidence versus Hospital-based Specialists.
†This number is statistically significant at 95% confidence versus Hospital-based Specialists and PCPs.
‡This number is statistically significant at 95% confidence versus Hospital-based Specialists and Gastroenterologists.

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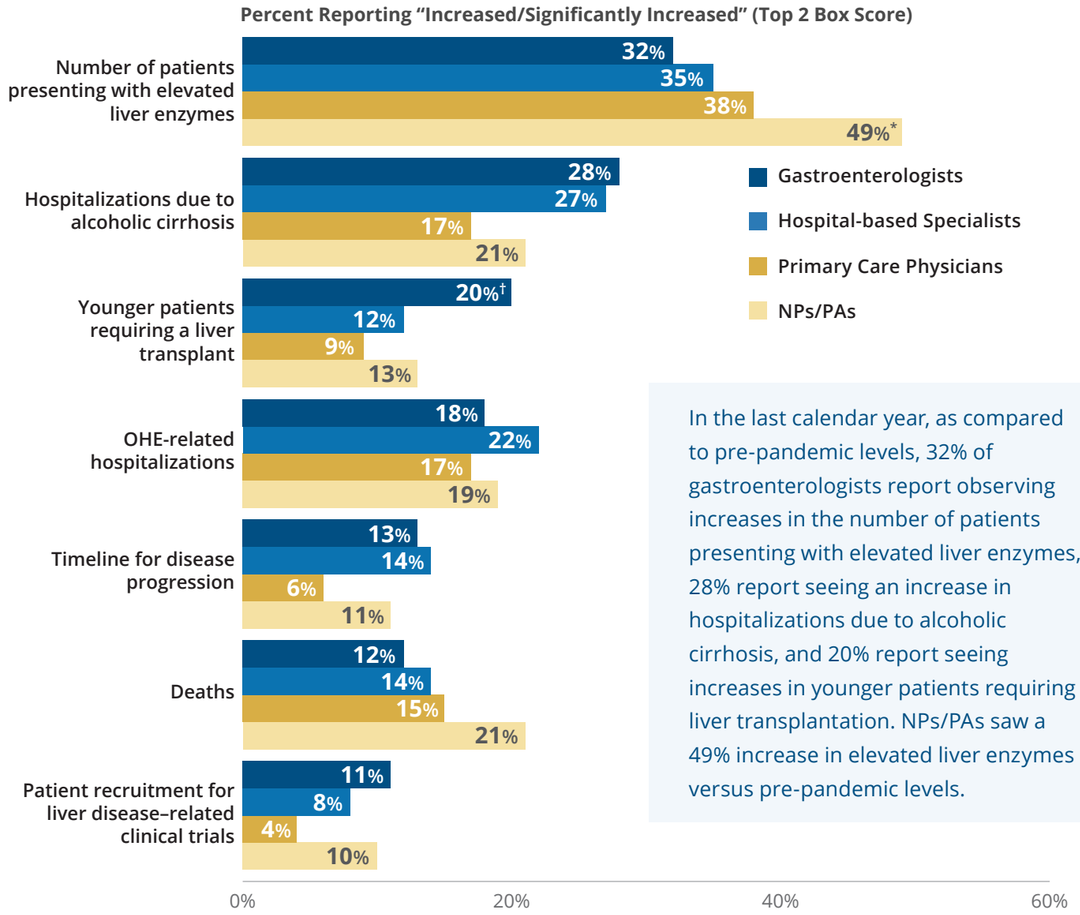
Figure 5 captures changes observed (increased/significantly increased) in respondents' adult patients living with liver disease as compared to pre-pandemic levels.

Figure 5 | **Changes Observed in Liver Disease–related Factors Versus Pre-pandemic Levels**

Q3.25. Please indicate any changes that you or your institution experienced as it pertains to your adult liver disease patients in the last calendar year as compared to 3 years ago (pre-pandemic). Please use a 7-point scale, where 1=significantly decreased and 7=significantly increased.



In the last calendar year, as compared to pre-pandemic levels, 32% of gastroenterologists report observing increases in the number of patients presenting with elevated liver enzymes, 28% report seeing an increase in hospitalizations due to alcoholic cirrhosis, and 20% report seeing increases in younger patients requiring liver transplantation. NPs/PAs saw a 49% increase in elevated liver enzymes versus pre-pandemic levels.

N=400 (100 Gastroenterologists, 100 Hospital-based Specialists, 100 PCPs, 100 NPs/PAs).
*This number is statistically significant at 95% confidence versus Gastroenterologists and Hospital-based Specialists.
†This number is statistically significant at 95% confidence versus PCPs.

"What I've seen in the literature is a correlation between COVID, not only among patients experiencing prolonged episodes of COVID 19 symptoms but also among those with acute episodes as well.."

—Gastroenterologist

"COVID is definitely still ongoing. We are still trying to catch up on pretty much everything—endoscopies, colonoscopies, office visits, everything. We are still way, way, way behind."

—Gastroenterologist

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Disparities in Care

Key Findings:

SECONDARY RESEARCH FROM PEER-REVIEWED PUBLICATIONS

The modeling analysis predicts shortages in 2023, 2028, and 2033 of 10%, 23%, and 35% clinical full-time employees, respectively, in adult hepatology.[17]

The AASLD Workforce Study Group used an integrated workforce framework model, which combined socioeconomic factors that drive economic demand, epidemiological factors that drive need, and utilization rates that incorporated the current use of health care services.[17]

Primary data were collected using an electronic survey of AASLD members and current hepatology fellows in training. Four-hundred seventy-five respondents who spent 50% or more of their time practicing hepatology responded to the survey.[17]

PRIMARY MARKET RESEARCH

Socioeconomic Factors

This year, all socioeconomic factors impacting liver disease patient outcomes experienced statistically significant increases in their importance ratings as compared to 2022 (at 95% confidence). For example, food security rose 53%. **[Figure 6]**

Staffing Shortages

Overall, 72% of all respondents report that their organizations have suffered chronic staffing shortages across many roles. Eighty percent of respondents report chronic nursing shortages within their organizations. A lesser 29% report shortages of gastroenterologists, and 26% report shortages of hepatologists. **[Figure 7]**

Respondents report that shortages in hepatologists and gastroenterologists have the greatest impact on their organization's ability to manage liver disease patient care (82% and 77%, respectively). **[Figure 7]**

Respondents working in rural settings reported 43% higher shortages of primary care physicians (PCPs) in their organizations versus respondents working in an urban/suburban setting at 28% (at 95% confidence).

Access to Care

Seventy-two percent of nurse practitioners/physician assistants (NPs/PAs) and 58% of PCPs report that long wait times are the top barrier for their liver disease patients to access care from a specialist. Other access barriers include finding a liver disease specialist who accepts Medicaid and shortages of liver disease specialists in my area (54% and 56% of NPs/PAs, respectively). **[Figure 8]**

For respondents located in rural areas, the average wait time to see a liver disease specialist is 13.1 weeks with a standard deviation (SD) of 29.7 (indicating a wide variance in wait times [eg, wait times almost 1 year]) compared with 7.6 weeks (SD 6.5) for urban/suburban patients. **[Figure 9]**

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In telephone interviews, respondents confirm that wait times to see a liver disease specialist are longer than usual. The increases are attributed to:

- Staff and specialist shortages
- Still catching up from pandemic lockdowns
- Increasing liver disease patient volumes
- New guidelines for colorectal screening which increased patient volumes

Multidisciplinary Care

Respondents report that approximately three-fourths of their patients with cirrhosis would benefit from receiving multidisciplinary care. Unfortunately, far less are receiving it. Respondents working in rural areas report that 34% of their patients with cirrhosis are receiving multidisciplinary care versus those in urban settings, who report 43% of patients getting this type of care. Access to multidisciplinary care is worse in rural versus urban settings, especially for respondents' patients with cirrhosis. **[Figure 10]**

Seventy-four percent of NPs/PAs report that "Provider shortages (eg, no appointments available or long wait times)" are the top reason that chronic liver disease (CLD) patients can not access multidisciplinary care (an increase of 54% versus last year). Respondents reported that the top 3 reasons that impede patients receiving multidisciplinary care are provider shortages, lack of patient motivation to seek appointments, and insurance status. **[Figure 11]**

For respondents not working in a hospital environment, less than 50% of multidisciplinary care partners share the same electronic health record (EHR) system. In telephone interviews, communication and patient continuity of care are thought to be enhanced in settings where providers and care partners share the same EHR system. **[Figure 12]**

Rural Versus Urban/Suburban Respondents

Survey data and telephone interviews pointed to disparities in care for patients in rural versus urban/suburban locations. For example:

- Social and economic factors that impact liver disease patient outcomes (eg, health literacy, employment, financial constraints)
- Beyond reporting shortages of liver disease specialists, respondents working in rural settings reported 43% higher shortages of PCPs in their organizations versus respondents working in an urban/suburban setting at 28% (at 95% confidence).
- While disparities of care can and do happen in all parts of the country, several issues were amplified in the survey results of those providers working in rural locations. For example, for providers working in rural locations, the average wait time for a patient to see a liver disease specialist was almost double at 13.1 weeks with an SD of 29.7 (indicating a wide range [eg, wait times up to 1 year]) compared with 7.6 weeks (SD 6.5) for urban/suburban locations. **[Figure 9]**

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- Lower respondent awareness of guidelines (eg, cirrhosis) **[Figure 19]**
- Less protocols/guidelines for liver disease embedded in their EHR **[Figure 34]**
- Reduced access to ancillary services (eg, clinical research) **[Figure 37]**

Please see the Methodology (page 10 of this report) Limitations of Market Research and Statistical Analysis section.

New Fatty Liver Disease Nomenclature Announced in June 2023[6]

- **Steatotic liver disease (SLD)**—overarching term to encompass the various etiologies of steatosis
- **Metabolic dysfunction–associated steatotic liver disease (MASLD)**—formerly nonalcoholic fatty liver disease (NAFLD); encompasses patients who have hepatic steatosis and have at least 1 of 5 cardiometabolic risk factors
- **Metabolic alcohol-associated liver disease (MetALD)**—those with MASLD who consume greater amounts of alcohol per week (140 g to 350 g/week and 210 g to 420 g/week for females and males, respectively)
- **Cryptogenic SLD**—those with no metabolic parameters and no known cause
- **Metabolic dysfunction–associated steatohepatitis (MASH)**—formerly nonalcoholic steatohepatitis (NASH)

Socioeconomic Factors: The Association of Food Insecurity and NAFLD

SECONDARY RESEARCH FROM PEER-REVIEWED PUBLICATIONS

The association of food insecurity (not having access to sufficient food, or food of an adequate quality to meet one's basic needs) with NAFLD was evaluated among low-income adults in the United States. A cross-sectional analysis of a nationally representative sample of adults from the NHANES (2005-2014 waves) was performed. Participants included adults in low-income households (≤200% of the federal poverty level) without chronic viral hepatitis or self-reported heavy alcohol use.[18]

In the multivariable model, food-insecure adults were more likely to have[18]:

- NAFLD (unadjusted odds ratio [OR] 1.14; 95% confidence interval [CI]: 0.93, 1.40); (adjusted OR: 1.38; 95% CI: 1.08, 1.77)
- Advanced fibrosis (unadjusted odds ratio [OR] 0.91; 95% confidence interval [CI]: 0.57, 1.45); (adjusted OR: 2.20; 95% CI: 1.27, 3.82) compared with food-secure adults

In the sensitivity analysis, food insecurity was also associated with higher odds of[18]:

- Obesity (adjusted OR: 1.32; 95% CI: 1.06, 1.66)
- Diabetes (adjusted OR: 1.41; 95% CI: 0.999, 1.982)

Food insecurity may be associated with NAFLD and advanced fibrosis. While no significant differences were found in unadjusted prevalence of NAFLD and advanced fibrosis among food secure or insecure adults, a significant difference was noted after adjusting for sociodemographic and behavioral factors.

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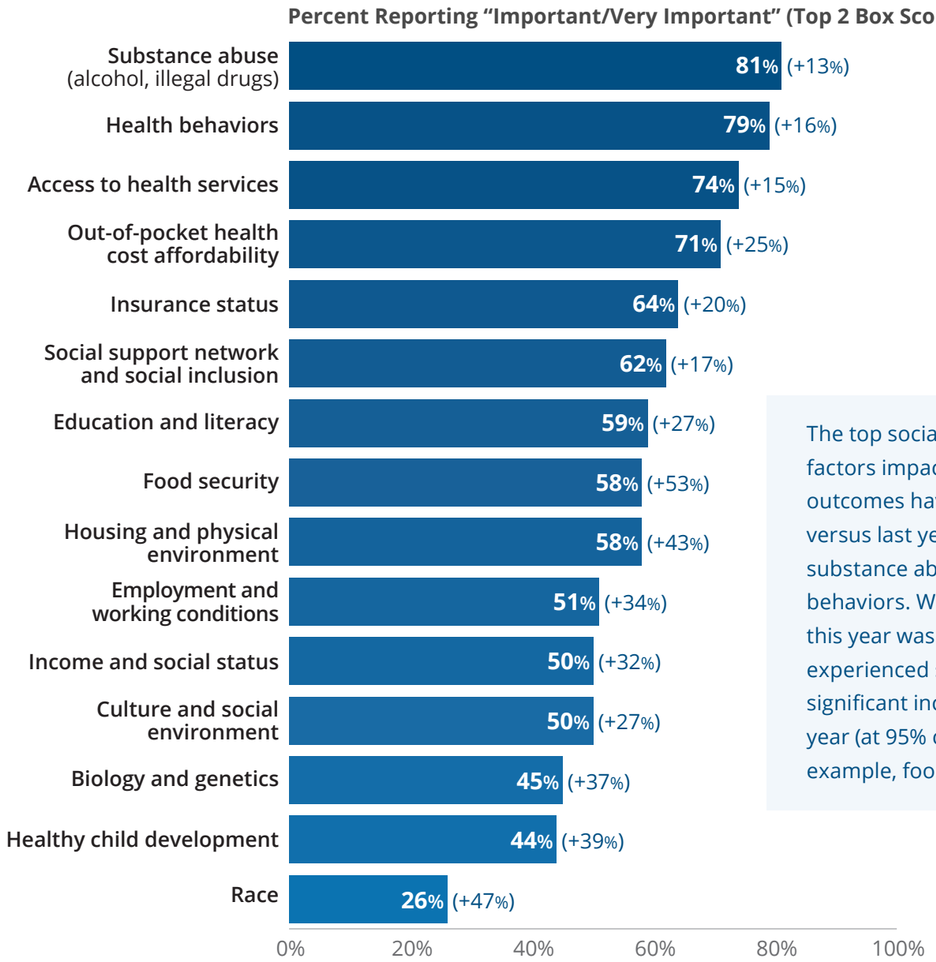
PRIMARY MARKET RESEARCH

Figure 6 shows the most important social/economic factors impacting CLD patient outcomes.

Figure 6 | **Most Important Social/Economic Factors Impacting CLD Patient Outcomes**

Q1. In your patient population, please rate the importance of the following social or economic factors on the health outcomes of your chronic liver disease patient population. Please use a 7-point scale, where 1=not at all important and 7=very important.



The top social and economic factors impacting CLD patient outcomes have not changed versus last year, leading with substance abuse and health behaviors. What was remarkable this year was that every factor experienced statistically significant increases versus last year (at 95% confidence). For example, food security rose 53%.

N=400 (100 Gastroenterologists, 100 Hospital-based Specialists, 100 PCPs, 100 NPs/PAs).
*All of the data points are statistically significant at 95% confidence versus last year.
Values in parentheses indicate percent change from 2022.

"Many of my patients are immigrants from countries that did not have any testing or prevention of hepatitis B. Unfortunately, some of them actually have progressed into fibrosis and cirrhosis."

—Gastroenterologist

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Staffing Shortages

SECONDARY RESEARCH FROM PEER-REVIEWED PUBLICATIONS

A 2018 predictive model from the American Association for the Study of Liver Diseases (AASLD) workforce study group reported a critical shortage of hepatology providers. They identified about 8000 gastroenterologists, hepatologists, and advanced practice providers (APPs) who had practices in which at least half of their time was spent in hepatology.[17] The modeling analysis predicts shortages in 2023, 2028, and 2033 of 10%, 23%, and 35% clinical full-time employees, respectively, in adult hepatology (see Table 2).[17]

Several factors influenced the demand, including[17]:

- Health care utilization patterns
- Prevalence of disease
- Changes in patient demographics
- Changes in geographic trends (ie, metropolitan statistical areas, net migrations, geographic mobility)
- Prevalence of liver disease
- Health care usage trends
- Practice trends
- Per capita income
- Aging of the population

The shift in care of patients with liver disease may fall not only to transplant hepatologists but also to APPs or other clinicians, such as primary care providers.[17]

Table 2 | **Projected Liver Disease Demand and Adult Hepatology Workforce Projections, 2018-2033[17]**

	2018 Baseline	2023 Projection	2028 Projection	2033 Projection
Total projected adults with liver disease	8,380,400	9,386,048	10,116,982	11,240,876
Total projected children with liver disease	1,833,000	1,935,648	2,022,914	2,104,208
MD (Clinical FTE)	5312	4825	4064	3349
NP (Clinical FTE)	682	723	723	766
PA (Clinical FTE)	138	146	155	164

FTE=full-time equivalent; MD=hepatologist or gastroenterologist who practices 50% or more hepatology; NP=nurse practitioner; PA=physician assistant.

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PRIMARY MARKET RESEARCH

Chronic staffing shortages were reported by 72% of all respondents who participated in this study. Figure 7 shows roles with the greatest impact on liver disease patient care.

Overall, 72% of all respondents report that their organizations have suffered chronic staffing shortages across many roles.

Eighty percent of respondents report chronic nursing shortages. A lesser 29% report shortages of gastroenterologists, and 26% report shortages of hepatologists.

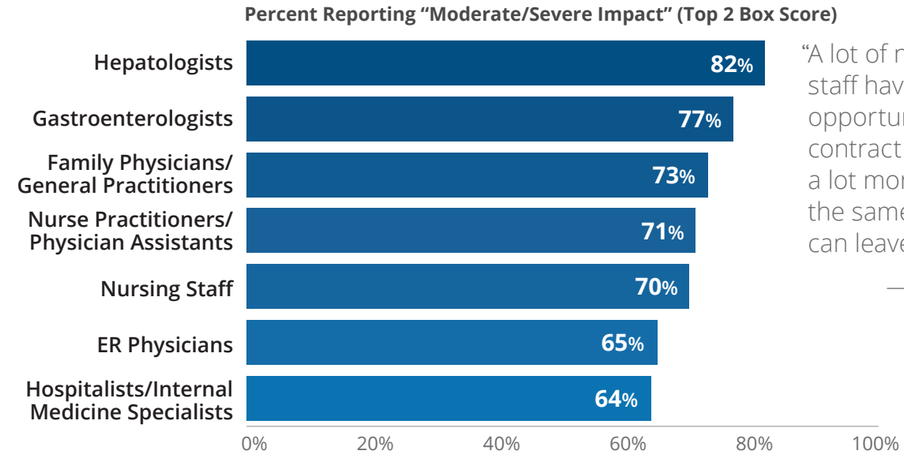
Respondents report that shortages in hepatologists and gastroenterologists have the greatest impact on their organization's ability to manage liver disease patient care (82% and 77%, respectively).

Respondents working in rural settings reported 43% higher shortages of PCPs versus respondents working in an urban/suburban setting at 28% (at 95% confidence).

Please see the Methodology (page 10 of this report) Limitations of Market Research and Statistical Analysis section.

Figure 7 | **Provider Roles With the Greatest Impact on Liver Disease Patient Care**

Q3.13. In what roles have the greatest shortages occurred? To what degree, if any, have these shortages impacted your organization's ability to manage patients living with liver disease? Please use a 5-point scale, where 1=no impact at all and 5=severe impact.



N=400 (100 Gastroenterologists, 100 Hospital-based Specialists, 100 PCPs, 100 NPs/PAs).

"A lot of nurses and support staff have taken the opportunity for traveling contract positions. It offers a lot more flexibility with the same amount of pay. It can leave us short-staffed."

—Gastroenterologist

"We are an academic institution in an urban area, but it is hard to attract gastroenterologists here. We could use a couple more, but it is getting harder to attract them. The school districts are not great."

—Gastroenterologist

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"It is widely recognized that there is a health care provider shortage (from medical assistants [MAs] to physicians and everything in between). This is going to be felt in our GI clinics, especially given that the survey confirmed an increase in the number of patients presenting with increased liver enzymes, the expected increase in fatty liver disease patients. It will be a huge burden in underserved areas where socioeconomic factors enrich the population in liver disease but there are far fewer clinicians with liver disease expertise. We are going to need to figure out alternative ways to manage these patients, as we do not have the infrastructure currently."

—Nancy Reau, MD, expert panelist

"There are tremendous disparities across the different settings I work in. The public hospital, for example, has 10 times the number of alcohol problems that we see in the not-for-profit hospital. The patient populations are very different; the insurance, as you can imagine, is very different; and there's a tremendous difference in stress."

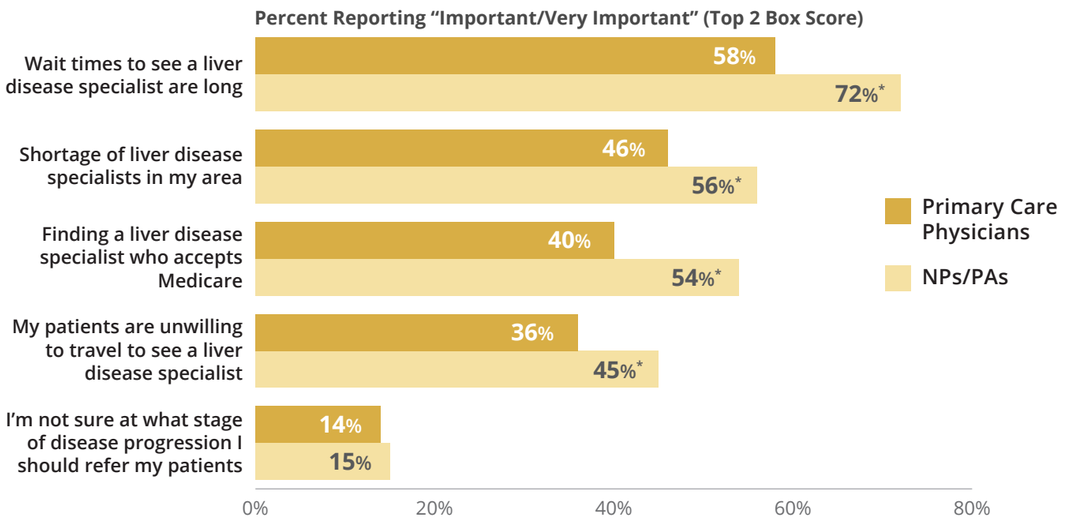
—Gastroenterologist

72% of NPs/PAs and 58% of PCPs report that long wait times are the top barrier for their liver disease patients to access care from a specialist. Other access barriers include finding a liver disease specialist who accepts Medicaid and shortages of liver disease specialists in my area (54% and 56% of NPs/PAs, respectively).

Figure 8 shows the factors most commonly impacting patient access to liver disease specialists.

Figure 8 | **Factors Impacting Patient Access to Liver Disease Specialists**

Q3.15. In your opinion, to what degree do the following factors impact your patients' ability to access a liver disease specialist? Please use a 7-point scale, where 1=not at all important and 7=very important.



N=200 (100 PCPs, 100 NPs/PAs).
*This number is statistically significant at 95% confidence versus PCPs.

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"It is a 6-month wait to see a gastroenterologist. Unless it is urgent or end-stage and then we can often call and talk to the clinic, and we can get patients in within a month."

—Primary care physician

"In a perfect world we would be able to send all our patients with a chronic GI issue to the GI Clinic, but because our access is so poor, that's just not possible. We can only send our highest-risk patients."

—Primary care physician

Figure 9 shows the average wait time to see a liver disease specialist.

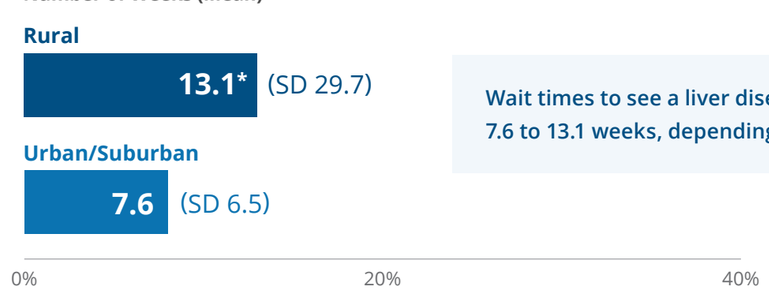
For respondents located in rural areas, the average wait time to see a liver disease specialist is 13.1 weeks with an SD of 29.7 (indicating a wide variance in wait times [eg, wait times almost 1 year]) compared with 7.6 weeks (SD 6.5) for urban/sububurban patients.

In telephone interviews, respondents confirm that wait times to see a liver disease specialist are longer than usual. The increases are attributed to:

- **Staff and specialist shortages**
- **Still catching up from pandemic lockdowns**
- **New guidelines for colorectal screening which increased patient volumes**
- **Increasing patient volumes**

Figure 9 | **Average Wait Time to See a Liver Disease Specialist**

Q3.16. On average, in your practice area, how many weeks does a patient have to wait to get in to see a liver disease specialist?



Wait times to see a liver disease specialist are, on average, 7.6 to 13.1 weeks, depending on where you live.

N=400 (356 urban/suburban providers, 44 rural providers).
*This number is statistically significant at 95% confidence versus urban/suburban providers.
The numbers in parentheses indicate the standard deviation (SD) for these values.

"We do find that our wait times to see patients have become a big issue. We have had to hire some mid-level providers to help kind of bridge the gap. I worry that this will impact our ratings because patients are not actually seeing a doctor."

—Rural internist

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Multidisciplinary Care

PRIMARY MARKET RESEARCH

Figure 10 shows the percent of respondents' patients that would benefit from and/or are receiving multidisciplinary care.

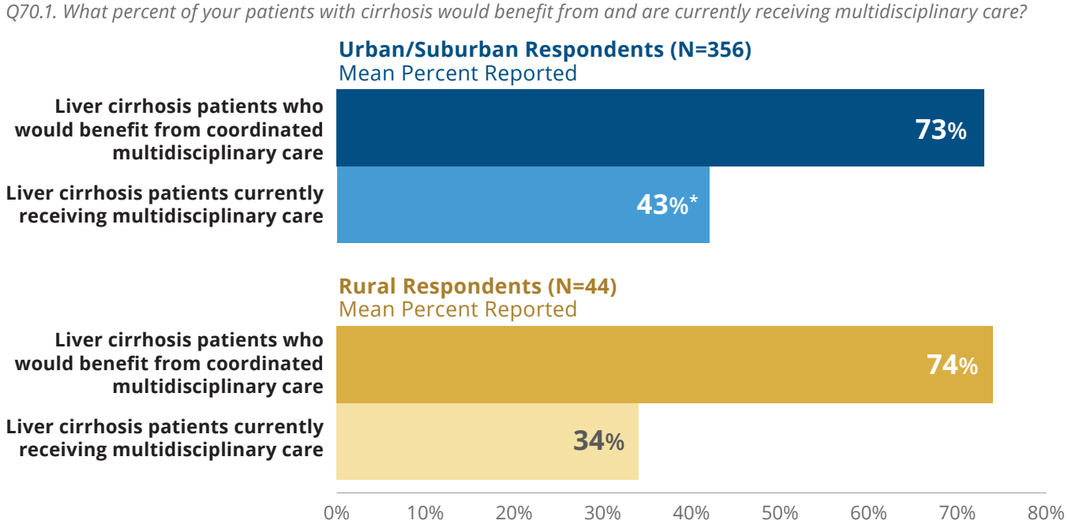
"I refer patients with end-stage liver disease or cirrhosis or advanced stage fibrosis to our liver center. Unfortunately, scheduling is a problem because it's a large referral center. Usually, my patients are seen within a week or sooner, but for those that are not acute, it can take 30 to 60 days."

—Internist

Respondents report that approximately three-fourths of their patients with cirrhosis would benefit from receiving multidisciplinary care. Respondents working in rural areas report that 34% of their patients with cirrhosis are receiving multidisciplinary care versus those in urban settings, who report 43% of patients getting this type of care. Access to multidisciplinary care is worse in rural versus urban settings, especially for respondents' patients with cirrhosis. **[Figure 10]**

Figure 10 | **Percent of Cirrhosis Patients Eligible for and/or Receiving Multidisciplinary Care**

Q70.1. What percent of your patients with cirrhosis would benefit from and are currently receiving multidisciplinary care?



N=400 (100 Gastroenterologists, 100 Hospital-based Specialists, 100 PCPs, 100 NPs/PAs [356 practicing in an urban/suburban setting versus 44 in a rural setting]).

*This number is statistically significant at 95% confidence versus the rural respondents.

Note: The market research and statistical analysis in this report were conducted in a manner consistent with industry standards and market research codes of conduct; however, this is in no way comparable to the scientific rigor of clinical research. All statistical significance in this report is at 95% confidence.

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Figure 11 shows factors that most frequently impede patients from receiving multidisciplinary care.

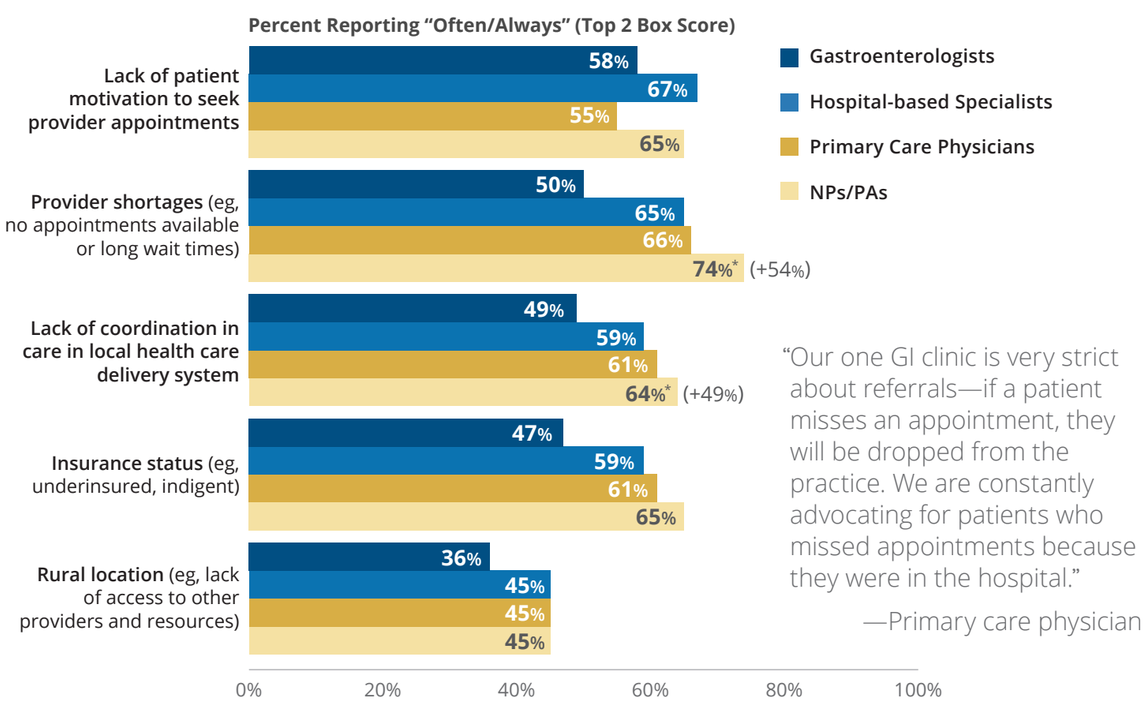
74% of NPs/PAs report that "Provider shortages" are the top reason that CLD patients cannot access multidisciplinary care (a statistically significant increase of 54% versus last year).

Respondents reported that the top 3 reasons that impede patients receiving multidisciplinary care are provider shortages, lack of patient motivation to seek appointments, and insurance status.

- Patients' reasons for refusing to see specialists include the following:
  - Travel outside their geographical area
  - Didn't want to leave their primary care doctor
  - Language barriers
  - Pay higher co-pays and other cost-related issues

Figure 11 | **Factors That Most Frequently Impede Patients From Receiving Multidisciplinary Care**

Q71. How frequently do the following factors prevent your patients from receiving coordinated multidisciplinary care (eg, primary care, specialists, dietitian, psychosocial support)?



N=400 (100 Gastroenterologists, 100 Hospital-based Specialists, 100 PCPs, 100 NPs/PAs).

*This number is statistically significant at 95% confidence versus last year.

Values in parentheses indicate percent change from 2022.

"Our one GI clinic is very strict about referrals—if a patient misses an appointment, they will be dropped from the practice. We are constantly advocating for patients who missed appointments because they were in the hospital."

—Primary care physician

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"Fortunately for patients who have liver disease and various comorbidities we have colleagues to refer to. I've worked at different places where it felt much harder to coordinate care for those populations because the delays, like needing interpreters."

—Gastroenterologist

"Sometimes our patients won't visit the liver doctor, so I'm communicating over the electronic medical record [EMR], and I'm leading and directing the care such that I become a specialist, so location is a barrier."

—Gastroenterologist

Figure 12 shows the percent of multidisciplinary care partners share the same EHR system.

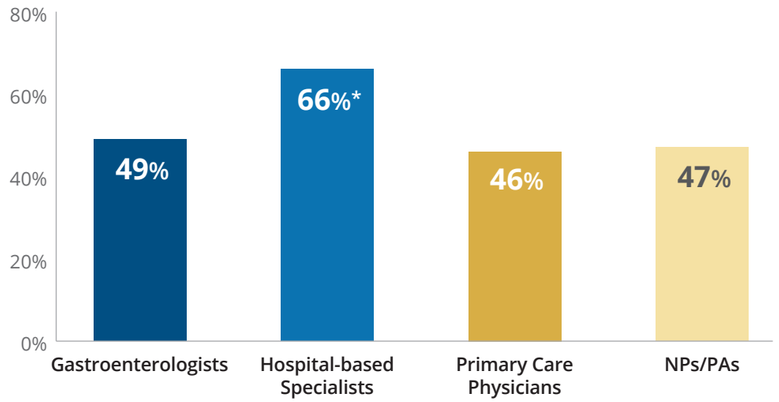
For respondents not working in a hospital environment, less than 50% of multidisciplinary care partners share the same EHR system.

In telephone interviews, communication and patient continuity of care is thought to be enhanced in settings where providers and care partners share the same EHR system.

Please see the Methodology (page 10 of this report) Limitations of Market Research and Statistical Analysis section.

Figure 12 | **Percent of Multidisciplinary Care Partners Sharing the Same EHR System**

Q3.18. What percent of the multidisciplinary care team that you utilize share the same EHR system as you?



N=400 (100 Gastroenterologists, 100 Hospital-based Specialists, 100 PCPs, 100 NPs/PAs).
*This number is statistically significant at 95% confidence versus all others.

"It is definitely easier if we are on the same EHR as the GI—continuity of care is better if we can see each other's notes."

—Primary care physician

"Part of the reason communication has improved [with other providers] is the EMR, which allows all of us on the same network to get information on an individual patient immediately."

—Gastroenterologist

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Urban/Suburban Versus Rural

PRIMARY MARKET RESEARCH

Survey data and telephone interviews pointed to disparities in care for patients in rural versus urban/suburban locations. For example:

- Social and economic factors that impact liver disease patient outcomes (eg, health literacy, employment, financial constraints) **[Figure 6]**
- Beyond reporting shortages of liver disease specialists, respondents working in rural settings reported 43% higher shortages of PCPs in their organizations versus respondents working in an urban/suburban setting at 28% (at 95% confidence).
- While disparities of care can and do happen in all parts of the country, several issues were amplified in the survey results of those providers working in rural locations. For example, for providers working in rural locations, the average wait time for a patient to see a liver disease specialist was almost double at 13.1 weeks with an SD of 29.7 (indicating a wide range [eg, wait times almost 1 year]) compared with 7.6 weeks (SD 6.5) for urban/suburban locations. **[Figure 9]**
- Lower respondent awareness of guidelines (eg, cirrhosis) **[Figure 19]**
- Less protocols/guidelines for liver disease embedded in their EHR **[Figure 34]**
- Reduced access to ancillary services (eg, clinical research) **[Figure 37]**

"In my rural area there's poor healthcare literacy, and maybe a low level of trust of the healthcare system. I see a lot of farmers and blue-collar working folks, probably financial constraints exist as well."

—Internist

"We are located in a rural area, so access to specialized care is limited. We have to ask our patients who are really, really sick to make the journey to a tertiary center that has the ability to do some of these more advanced workups and transplant evaluations. Given the financial resources of some of our patients, that seems to be difficult for them."

—Internist

"The biggest barriers to getting multidisciplinary care for my patients is the time it takes to get an appointment with a liver disease specialist. And patients can be reluctant if the co-pay is more than what they pay to see us."

—Primary care physician

Note: The market research and statistical analysis in this report were conducted in a manner consistent with industry standards and market research codes of conduct; however, this is in no way comparable to the scientific rigor of clinical research. All statistical significance in this report is at 95% confidence.

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Care Management

Key Findings:

SECONDARY RESEARCH FROM PEER-REVIEWED PUBLICATIONS

Telephonic Transitional Care Program Improves Cirrhosis Survival

A hepatic encephalopathy (HE) outpatient telephonic transitional care (OTTC) program involved telephone-based follow-up, active monitoring of diagnostic tests, coordination of outpatient care, and disease- and medication-related counseling. Survival was compared between patients who received OTTC (n=76) versus those who did not (n=93) at 6 months.[19]

- Patients in the intervention group were 60% less likely to die than patients in the control group during the 6-month follow-up. The intervention group showed significantly higher 6-month survival compared with controls (84.2% versus 68.8%; P=0.03).[19]

The Majority of Patients With Cirrhosis Do Not Receive Evidence-based Care

A retrospective chart review from 2013 to 2018 of adult patients with cirrhosis seen in the outpatient setting observed[20]:

- Overall, 11 (3%) of the patients achieved all of the preventive quality indicators (QIs) for which they were eligible, and 61 (14%) achieved greater than 75% of eligible QIs. QIs included preventive care for ascites, esophageal varices, hepatic encephalopathy, hepatocellular carcinoma, and general cirrhosis care.

Advanced Practice Providers (APPs) Can Meet the Challenges of Cirrhosis Care

Using a retrospective analysis of a nationally representative American commercial claims database compared patients with cirrhosis without APP care (n=222,549) to patients with APP care (N=166,708)[21]

- Patients with cirrhosis under the care of an APP had a reduced risk of death (adjusted HR: 0.57; 95% confidence interval [CI]: 0.55, 0.60)

PRIMARY MARKET RESEARCH

Thirty-one percent of surveyed respondents, who treat liver disease, are unaware of any national guidelines for the management of CLD. **[Figure 15]**

The top 2 care management factors impacting chronic liver disease (CLD) patient outcomes are "Treating the acute condition" and "Patient's treatment adherence." **[Figure 13]**

Of note, there was a statistically significant increase of 34% in the importance of the use of third-party guidelines versus 2022 (44% to 59%). **[Figure 13]**

When choosing an intervention or treatment for CLD, respondents reported that "Treatment that reduces the risk of disease" and "Treatment is covered by insurance" were again the top 2 most important factors influencing treatment decisions. **[Figure 14]**

Adoption of Guidelines/Standardized Care/Quality Metrics

There were no significant changes in awareness of guidelines except primary care physicians (PCPs), who reported a statistically significant increase in awareness for cirrhosis guidelines, an increase of 27% versus last year (51% to 65%). **[Figure 15]**

Sixty-eight percent of respondents reported that it is important/very important to align their CLD treatment management with national treatment guidelines, a statistically significant increase of 13% versus last year. **[Figure 16]**

Of those who said they utilize national guidelines for liver disease care management (N=320), 56% of respondents say they are interested in these guidelines but not sure how to translate the information into daily practice, a statistically significant increase of 332% versus last year. **[Figure 17]**

Eighty percent of respondents report improving CLD patient outcomes as being the most important reason for providers to adopt guidelines. Other important factors included slowing disease progression and improving screening, prevention, and diagnosis of CLD complications. **[Figure 18]**

NASH and NAFLD

In telephone interviews, providers speak to the most challenging aspect: getting patients to understand their role in early liver disease management. They use innovative analogies and tools to impress upon their patients that the damage could be reversible if they act quickly.

Forty-three percent of respondents utilize the APRI (ALT-to-platelet ratio index) Score test to identify nonalcoholic steatohepatitis (NASH) or nonalcoholic fatty liver disease (NAFLD) patients, and 48% used the test to identify disease progression (eg, fibrosis, cirrhosis) in this patient population. **[Figure 20]**

Cirrhosis and Hepatic Encephalopathy

This year, PCPs were sending more Grade II patients (+65%) to the emergency room versus the previous years (at 95% confidence). **[Figure 23]**

Eighty-seven percent of respondents cite patient noncompliance as the most common factor that limits the duration of treatment to prevent HE recurrence. **[Figure 25]**

Thirty-two percent of respondents report that the inability to pay for medication post hospital discharge happens the most frequently (almost every time/every single time). **[Figure 29]**

Over 40% of respondents have readily adopted the dedicated ICD-10 code (K76.82) for HE. **[Figure 27]**

Please see the Methodology (page 10 of this report) Limitations of Market Research and Statistical Analysis section.

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Evolving Role of PCPs and NPs/PAs—Summary

Gastroenterologists and PCPs do not agree on who is best equipped to manage NAFLD:

- 77% of gastroenterologists report that a liver disease specialist is the best provider.
- 57% of PCPs believe that family physicians/general practitioners are the most appropriate provider. **[Figure 30]**

In the telephone interviews, there is agreement that primary care providers help patients access care when specialists' access is limited or prohibited; concern exists that optimal care may be compromised.

Patient Engagement

≥55% of respondents indicated strong agreement with the need for:

- Better tools to help them access current and future care needs (59%)
- Addressing unmet patient information needs to help improve patient engagement in care management and reduce anxiety (56%)
- Earlier integration of palliative care and community services (55%) **[Figure 33]**

Forty-four percent of respondents agree/strongly agree with the statement that "Patients often feel social stigma in their communities related to their liver disease." Many patients feel stigma due to misconceptions about how their liver disease occurred (eg, not knowing that it is not all alcohol related). **[Figure 33]**

Thirty-seven percent of respondents agree/strongly agree with the statement that "Patients often feel social stigma related to their diagnosis when meeting with their health care team." In telephone interviews, respondents suggested ways the medical community can reduce medical stigma (eg, stop using the terminology "fatty liver disease" but instead use NASH or NAFLD). **[Figure 33]**

New Fatty Liver Disease Nomenclature Announced in June 2023[6]

- **Steatotic liver disease (SLD)**—overarching term to encompass the various etiologies of steatosis
- **Metabolic dysfunction–associated steatotic liver disease (MASLD)**—formerly nonalcoholic fatty liver disease (NAFLD); encompasses patients who have hepatic steatosis and have at least 1 of 5 cardiometabolic risk factors
- **Metabolic alcohol-associated liver disease (MetALD)**—those with MASLD who consume greater amounts of alcohol per week (140 g to 350 g/week and 210 g to 420 g/week for females and males, respectively)
- **Cryptogenic SLD**—those with no metabolic parameters and no known cause
- **Metabolic dysfunction–associated steatohepatitis (MASH)**—formerly nonalcoholic steatohepatitis (NASH)

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PRIMARY MARKET RESEARCH

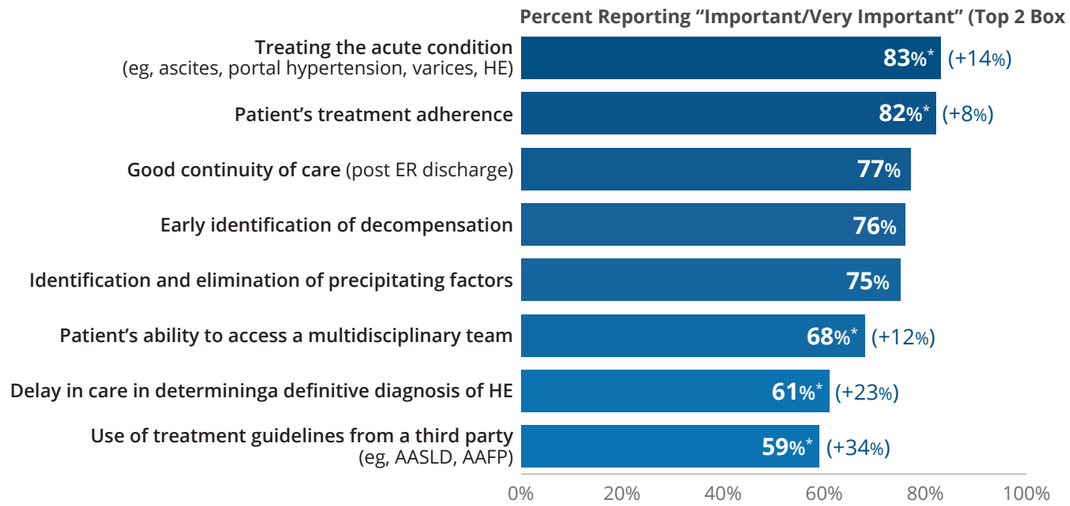
Figure 13 shows the importance ratings on care management interventions and their impact on liver disease patient outcomes.

The top 2 care management factors impacting CLD patient outcomes are "Treating the acute condition" and "Patient's treatment adherence"—both had statically significant increases in their importance ratings versus last year. In telephone interviews, respondents expressed how challenging it is to get patients to engage in treatment for early-stage liver disease (NASH/NAFLD).

Of note, there was a statistically significant increase of 34% in the importance of the use of third-party guidelines versus 2022 (44% to 59%).

Figure 13 | **Importance of Care Management on Liver Disease Patient Outcomes**

Q3. Please rate the importance of each of these factors with respect to their impact on chronic liver disease patient outcomes. Please use a 7-point scale, where 1=not at all important and 7=very important.



N=400 (100 Gastroenterologists, 100 Hospital-based Specialists, 100 PCPs, 100 NPs/PAs).
*This number is statistically significant at 95% confidence versus last year.
Values in parentheses indicate percent change from 2022.

"It is important to recognize that treating the condition and adherence were flagged as the most important management factors. Guidelines and quality metrics are directly tied to both of these factors, and guideline awareness among providers continues to be low.

- We need to find a better way to disseminate national guidelines. Clinicians want to align management with these resources but lack the time/means to find and read them.
- Our national guidelines may also not be the tool they believe they are. Many clinicians could not translate the information into their practice. This feedback is important for our guideline committees."

—Nancy Reau, MD, expert panelist

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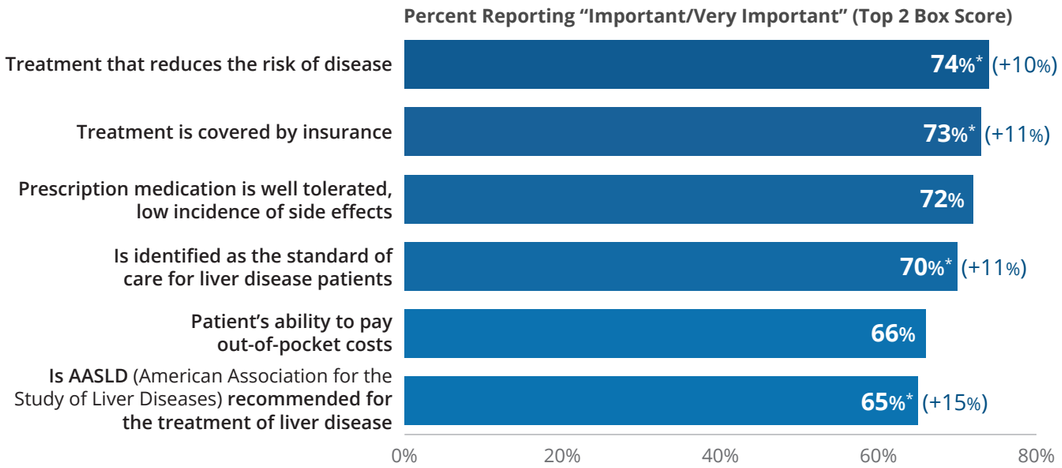
Figure 14 speaks to the most important factors considered when making treatment decisions for CLD patients.

When choosing an intervention or treatment for CLD, respondents reported that "Treatment that reduces the risk of disease" and "Treatment is covered by insurance" were again the top 2 most important factors influencing treatment decisions (each receiving statistically significant increases over last year). Factors that reported higher importance ratings this year were ability to access multidisciplinary team members, delay in care getting an HE diagnosis, and use of treatment guidelines from a third party. **[Figure 14]**

Figure 14 | **Most Important Factors Considered When Making Treatment Decisions**

Q9. Please rate the importance of each of these factors when making treatment decisions for patients with chronic liver disease. Please use a 7-point scale, where 1=not at all important and 7=very important.



N=400 (100 Gastroenterologists, 100 Hospital-based Specialists, 100 PCPs, 100 NPs/PAs).
*This number is statistically significant at 95% confidence versus last year.
Values in parentheses indicate percent change from 2022.

"For my patients, homelessness and the ability to access specialty GI care are the biggest factors impacting my patients' outcomes."

—Primary care physician

Note: The market research and statistical analysis in this report were conducted in a manner consistent with industry standards and market research codes of conduct; however, this is in no way comparable to the scientific rigor of clinical research. All statistical significance in this report is at 95% confidence.

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Adoption of Guidelines/Standardized Care/Quality Metrics

PRIMARY MARKET RESEARCH

Figure 15 shows respondent awareness of national guidelines for the management of patients suffering from chronic liver disease.

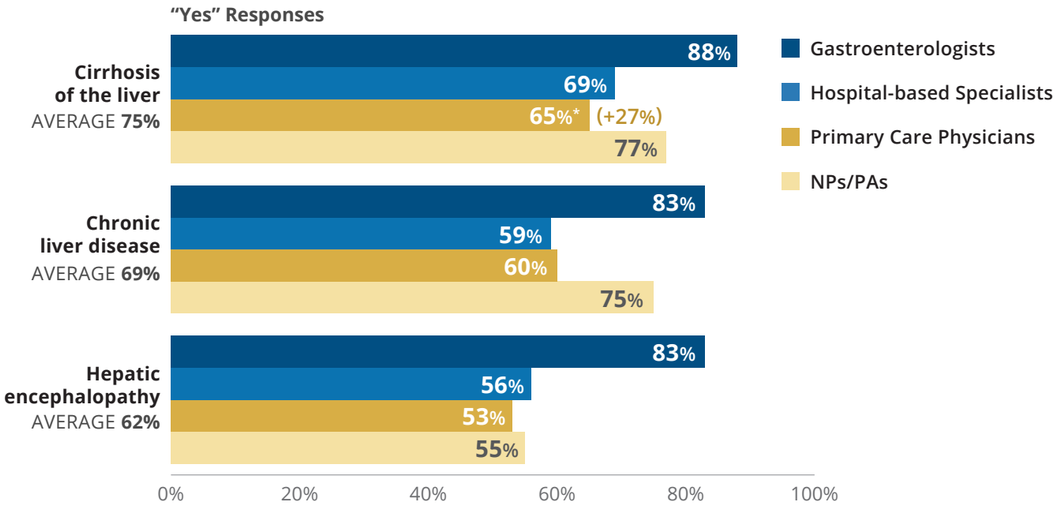
Thirty-one percent of surveyed respondents, who treat liver disease, are unaware of any national guidelines for the management of CLD. **[Figure 15]**

Gastroenterologists continue to have the highest awareness of national guidelines for liver disease management.

There were no significant changes in awareness of guidelines except PCPs, who reported a statistically significant increase in awareness for cirrhosis guidelines of 27% versus last year (51% to 65%).

Figure 15 | **Respondent Awareness of National Guidelines for Liver Disease Management**

Q5. Are you aware of any national guidelines for the management of patients suffering from chronic liver disease?



N size varies by answer.
*This number is statistically significant at 95% confidence versus last year.
Values in parentheses indicate percent change from 2022.

"I always use AASLD—the American Association for the Study of Liver Diseases. And then in general I'll use UpToDate or product-related information because it's built into the EMR [electronic medical record]."

—Primary care physician

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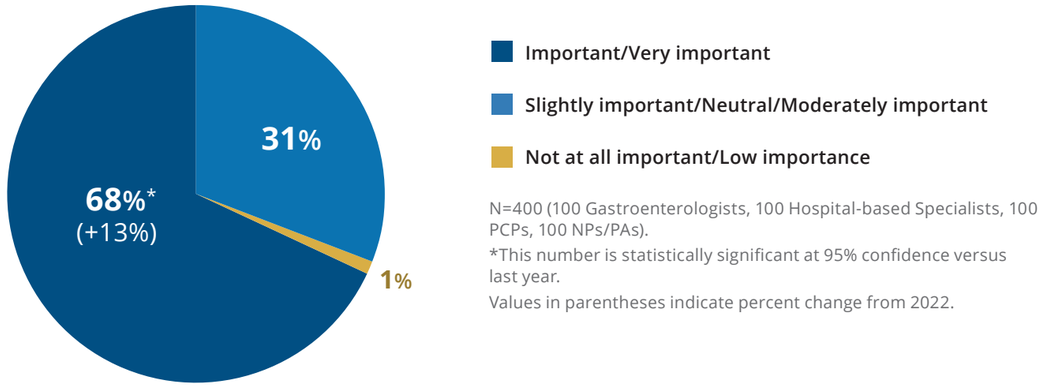
In Figure 16, respondents report on whether aligning their CLD treatment management with national treatment guidelines and quality metrics is important.

68% of respondents report that aligning their CLD treatment management with national treatment guidelines and quality metrics is important/very important (a statistically significant increase of 13% versus last year).

Figure 16 | **Importance of Aligning With National Treatment Guidelines and Quality Measures for CLD**

Q7. How important is it to you personally for your patient management to be aligned with national treatment guidelines and quality measures for chronic liver disease? Please use a 7-point scale, where 1=not at all important and 7=very important.



N=400 (100 Gastroenterologists, 100 Hospital-based Specialists, 100 PCPs, 100 NPs/PAs).
*This number is statistically significant at 95% confidence versus last year.
Values in parentheses indicate percent change from 2022.

"Guidelines and quality metrics for liver disease are currently being implemented in our hospital. Our goal is to improve clinical outcomes."

—Internist

"We have to tailor any kind of clinical guidelines to each patient—but, overall guidelines are very helpful and efficient. I try to apply them as close as possible to each patient."

—Internist

"The problem arises when there's a conflict between best practices and financial aspects. A good example of that is getting a NASH diagnosis. The best test we have is an MRI [magnetic resonance imaging], but it is very expensive and hard to get insurance coverage."

—Gastroenterologist

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Figure 17 shows how respondents incorporate national guidelines into care management.

Of those who said they utilize national guidelines for liver disease care management (N=320), 56% of respondents say they are interested in these guidelines but not sure how to translate the information into daily practice, a statistically significant increase of 332% versus last year.

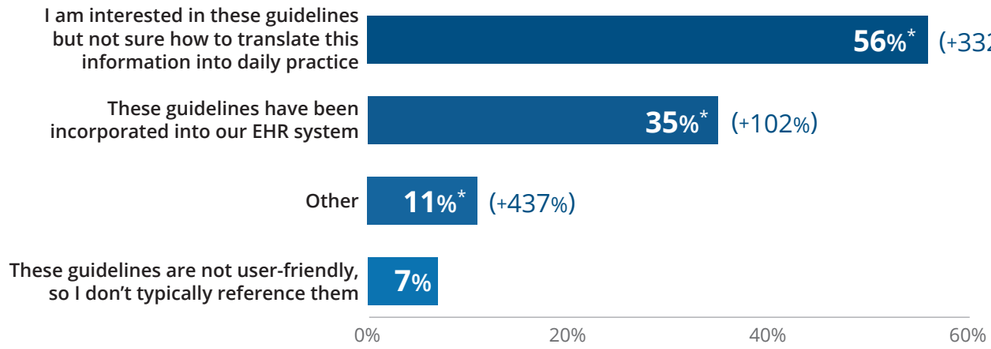
35% of respondents report that national guidelines have been incorporated into their electronic health record (EHR) system, a statistically significant increase of 102% over last year.

In telephone interviews, respondents felt that improvements needed to be made to national guidelines, which included:

- The use of noninvasive tests for a definitive NASH or NAFLD diagnosis
- Making the guidelines less "academic" and more user-friendly in the clinical setting

Figure 17 | **How National Guidelines Are Incorporated Into Care Management**

Q63. Please select the statements that best represent how you utilize these guidelines and/or pathways to manage your liver disease patients.



N=320 (92 Gastroenterologists, 77 Hospital-based Specialists, 71 PCPs, 80 NPs/PAs).
*This number is statistically significant at 95% confidence versus last year.
Values in parentheses indicate percent change from 2022.

"The monitoring guidelines are detailed for patients with biopsy-proven NASH, but if you do not have that, they just say recommend a reassessment every 3-4 years. I cannot imagine a circumstance where I would biopsy a patient to confirm that diagnosis—it's too invasive."

—Primary care physician

"I tend not to focus on the national guidelines as much because they are a little bit esoteric. I think they tend to be more academic than really helpful in a clinical setting."

—Gastroenterologist

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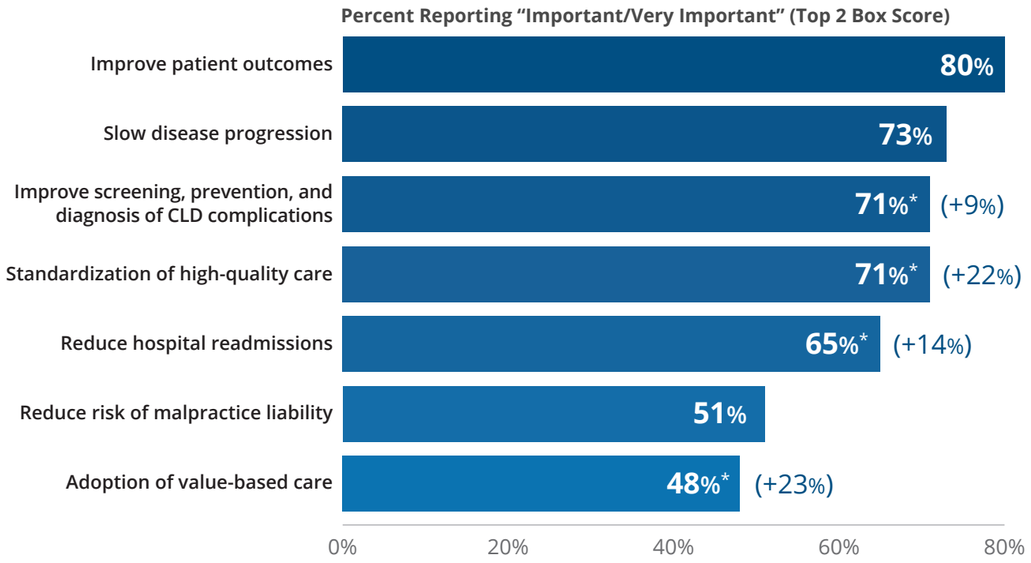
Figure 18 shows factors that are important in driving provider utilization of CLD guidelines.

80% of respondents report improving CLD patient outcomes as being the most important reason to adopt guidelines.

Figure 18 | **Factors Important in Driving Provider Utilization of Guidelines**

Q12. Please rate the following factors in order of their importance in driving provider use and adoption of chronic liver disease guidelines. Please use a 7-point scale, where 1=not at all important and 7=very important.



N=400 (100 Gastroenterologists, 100 Hospital-based Specialists, 100 PCPs, 100 NPs/PAs).
*This number is statistically significant at 95% confidence versus last year.
Values in parentheses indicate percent change from 2022.

"I was trained by someone who is in academia who was very big on evidence-based medicine and guidelines with the goal of improving patient outcomes. When I'm teaching my residents or an NP [nurse practitioner], I direct them toward the AASLD guidelines."

—Primary care physician

"We have protocols in the hospital, for example, hepatic encephalopathy or subacute bacterial peritonitis. If you don't follow the protocols, you have to have a reason in the EMR for not following them. It's looser in our private practice."

—Gastroenterologist

"Our management of liver disease doesn't feel as robust as, for example, our quality improvement related to heart failure readmission, right? I just discharged my patient, and they came back to the hospital 2 days later. But the hospital is not paying for that. I can't say we track that for liver disease in general."

—Primary care physician

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Figure 19 captures the percent of respondent organizations that have written guidance and/or quality measures for liver diseases.

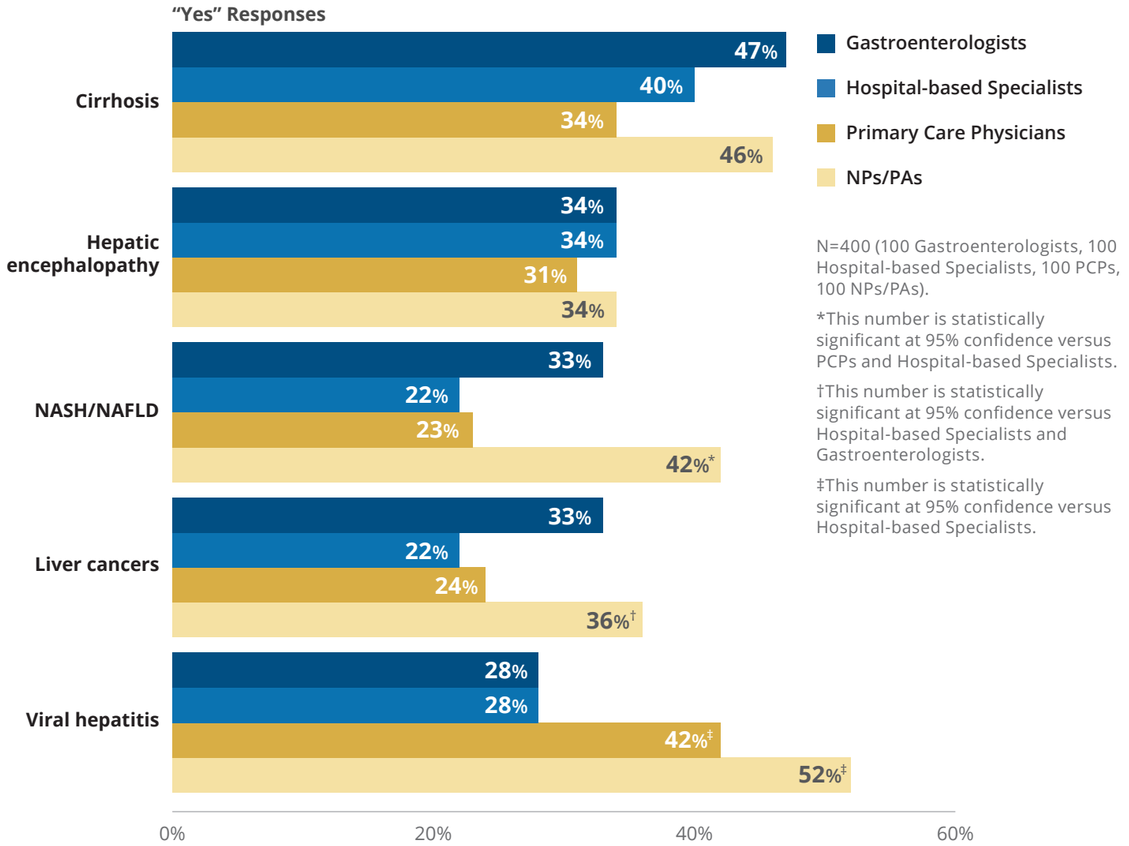
Overall, 42% of all respondents report having written guidance and/or quality metrics in their organizations.

Guidelines for cirrhosis appear most frequently in gastroenterologist and hospital-based specialist organizations, while PCPs and nurse practitioners/physician assistants (NPs/PAs) most frequently have guidelines for viral hepatitis.

Overall, written guidance and/or quality metrics are more prevalent for cirrhosis in respondents who are in urban/suburban locations versus rural (44% versus 25%, respectively, at 95% confidence).

Figure 19 | **Organizations Who Have Written Guidance and/or Quality Measures for Liver Diseases**

Q4. Does your organization have written guidance or quality measures for the following diseases of the liver?



N=400 (100 Gastroenterologists, 100 Hospital-based Specialists, 100 PCPs, 100 NPs/PAs).

*This number is statistically significant at 95% confidence versus PCPs and Hospital-based Specialists.

†This number is statistically significant at 95% confidence versus Hospital-based Specialists and Gastroenterologists.

‡This number is statistically significant at 95% confidence versus Hospital-based Specialists.

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NASH and NAFLD

PRIMARY MARKET RESEARCH

Figure 20 shows respondents' utilization of the APRI Score to screen their general population for the presence of NASH and/or NAFLD patients as well as to track disease progression in this patient population.

"You know, in the early stage, patients might not necessarily feel that they are sick. And so, with this limited knowledge about their liver disease or their risk factors or prevention strategies or the health care literacy issues, it just seems that there is a level of buy-in that is hard to get from these folks and an adherence to compliance with a treatment plan."

—Rural Internist

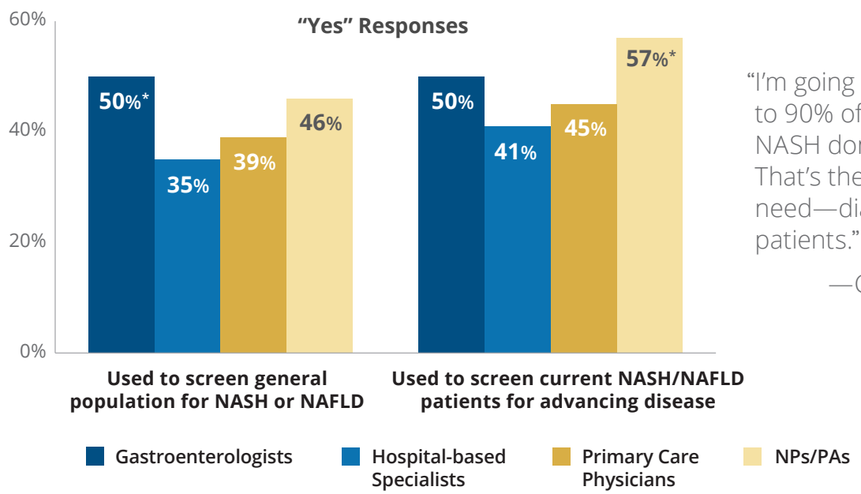
"We identify a lot of NASH. I have a 3D model of a liver in every exam room that shows the different stages of cirrhosis and fibrosis that helps me explain what early-stage disease is and how function is impaired as the liver issues worsen."

—Primary care physician

43% of respondents utilize the APRI Score test to identify NASH or NAFLD patients, and 48% used the test to identify disease progression (eg, fibrosis, cirrhosis) in this patient population.

Figure 20 | **Utilization of the APRI Score to Identify NASH/NAFLD and Disease Progression**

Q3.10. In your practice setting, do you utilize an APRI (ALT-to-platelet ratio index) Score to identify the following patients: (A) Used to screen general patient population for NASH or NAFLD (B) Used to screen current NASH/NAFLD patients for advancing disease?



"I'm going to guess that 75% to 90% of patients with NASH don't even know it. That's the greatest unmet need—diagnosing these patients."

—Gastroenterologist

N=400 (100 Gastroenterologists, 100 Hospital-based Specialists, 100 PCPs, 100 NPs/PAs).
*This number is statistically significant at 95% confidence versus Hospital-based Specialists.

"There is a strong desire to use noninvasive tools to screen and triage patients. Most guidelines suggest using FIB-4 (despite the lack of accuracy in those both young and old). In this survey, APRI was the most frequently used tool. I think it is important to understand why."

—Nancy Reau, MD, expert panelist

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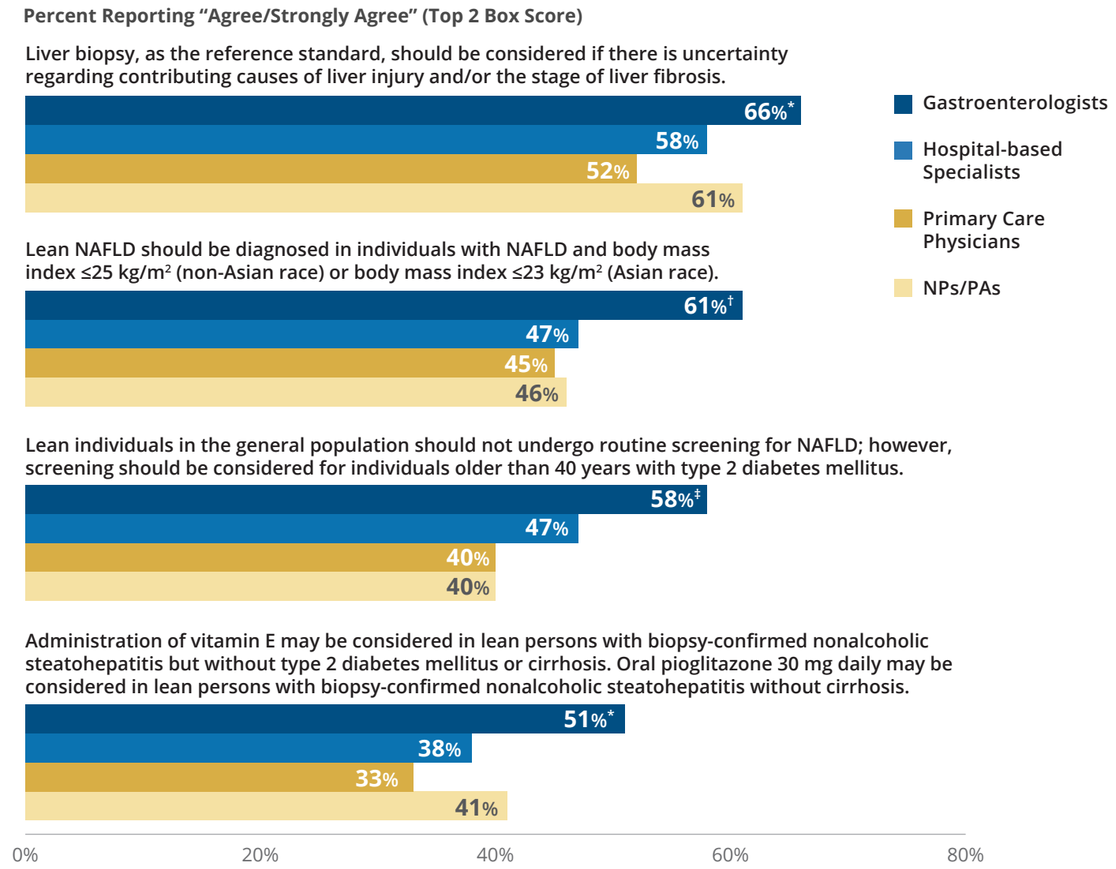
Figure 21 shows respondent agreement with the following statements relating to NAFLD patient management. The gastroenterologists' agreement (agree/strongly agree) was statistically higher than other provider groups (at 95% confidence).

Figure 21 | **Respondent Agreement With the Following Statements per NAFLD Patient Management**

Q3.11. Please indicate whether you agree or disagree with the following statements pertaining to the management of patients with NASH/NAFLD. Please use a 7-point scale, where 1=do not agree at all and 7=strongly agree.



N=400 (100 Gastroenterologists, 100 Hospital-based Specialists, 100 PCPs, 100 NPs/PAs).

*This number is statistically significant at 95% confidence versus PCPs.

†This number is statistically significant at 95% confidence versus all others.

‡This number is statistically significant at 95% confidence versus PCPs and NPs/PAs.

This question was adapted using the American Gastroenterological Association's best-practice guidelines for the management of NAFLD in lean individuals.[22]

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Cirrhosis and Hepatic Encephalopathy

SECONDARY RESEARCH FROM PEER-REVIEWED PUBLICATIONS

Telephonic Transitional Care Program Improves Cirrhosis Survival

The value of an outpatient telephone-based transitional care program in improving post hospital discharge in patients with cirrhosis was demonstrated in a 2016 study from a tertiary center.[19]

The cohort study included 169 patients with cirrhosis. The intervention group who received the outpatient OTTC was comprised of 76 patients and was compared with 93 controls.[19]

The OTTC program involved telephone-based follow-up, active monitoring of diagnostic tests, coordination of outpatient care, and disease- and medication-related counseling. Survival was compared between patients who received OTTC (n=76) versus those who did not (n=93) at 6 months.[19]

- Patients in the intervention group were 60% less likely to die than patients in the control group during the 6-month follow-up. The intervention group showed significantly higher 6-month survival compared with controls (84.2% versus 68.8%; P=0.03)

On multivariable analysis of demographic-, disease-, and hospitalization-related characteristics[19]:

- The intervention group showed lower odds for mortality compared with the controls (hazard ratio [HR]: 0.4; 95% CI: 0.2-0.82; P=0.012).
- Higher model for end-stage liver disease scores were associated with higher mortality (HR: 1.05; 95% CI: 1.01-1.1; P=0.024).

The Majority of Patients With Cirrhosis Do Not Receive Evidence-based Care

A retrospective chart review of adult patients with cirrhosis who were seen by an outpatient provider at least once at the University of California, Los Angeles (UCLA) Health System between January 1, 2013, and January 31, 2018 (n=439) was conducted. Patients were followed through January 31, 2019.[20]

The quality of outpatient preventive care was measured using 12 specific evidence-based preventive QIs.[20]

Overall, 11 (3%) of the patients achieved all of the QIs for which they were eligible, and 61 (14%) achieved greater than 75% of eligible QIs. QIs included preventive care for ascites, esophageal varices, hepatic encephalopathy, hepatocellular carcinoma, and general cirrhosis care.[20]

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General preventive care[20]

- Among the patients with cirrhosis, the percentage who received hepatitis A vaccinations, were recommended to receive the vaccination or had immunity in the chart: 51% (n=439)
- Among the patients with cirrhosis, the percentage who received hepatitis B vaccinations, were recommended to receive the vaccination or had immunity in the chart: 54% (n=416)
- Among the patients with alcohol-associated cirrhosis, the percentage who were counseled to abstain from alcohol consumption: 83% (n=136)
- Among the patients with moderate hepatic encephalopathy, the percentage who have received counseling for avoidance of driving: 5% (n=130)
- Among patients eligible for hepatocellular carcinoma surveillance, the percentage who received screening with imaging every 6 months (with a 1-month buffer): 24% (n=393)

Primary and secondary prevention of variceal bleeding[20]

- Among the patients with compensated cirrhosis at their initial GI/hepatology visit, the percentage who have been screened for varices with an esophagogastroduodenoscopy (EGD) within 12 months of their initial GI/hepatology visit or date of cirrhosis diagnosis: 32% (n=280)
- Among the patients with decompensated cirrhosis at their initial GI/hepatology visit, the percentage who have been screened for varices with an EGD within 3 months of their initial GI/hepatology visit or date of cirrhosis diagnosis: 61% (n=155)
- Among the patients with decompensated cirrhosis who have small varices on EGD and are not on nonselective beta-blockers (NSBBs), the percentage who have a repeat within 1 year: 45% (n=75)
- Among patients with cirrhosis and medium/large varices on endoscopy, the percentage who received either NSBBs or variceal ligation within 1 month of varices diagnosis: 75% (n=91)
- Among patients with cirrhosis and variceal bleeding, the percentage who had variceal ligation performed every 4 weeks until obliteration, beta-blockers, or a combination of variceal ligation and beta-blockers for secondary prevention: 2% (n=45)

Spontaneous bacterial peritonitis (SBP) prophylaxis[20]

- Among patients with cirrhosis and documented SBP, the percentage who were on long-term outpatient antibiotics: 21% (n=28)
- Among patients with cirrhosis, history of ascites, and ascitic fluid total protein <1.1 g/dL and serum total bilirubin >2.5 mg/dL, the percentage who were on long-term outpatient antibiotics: 9% (n=77)

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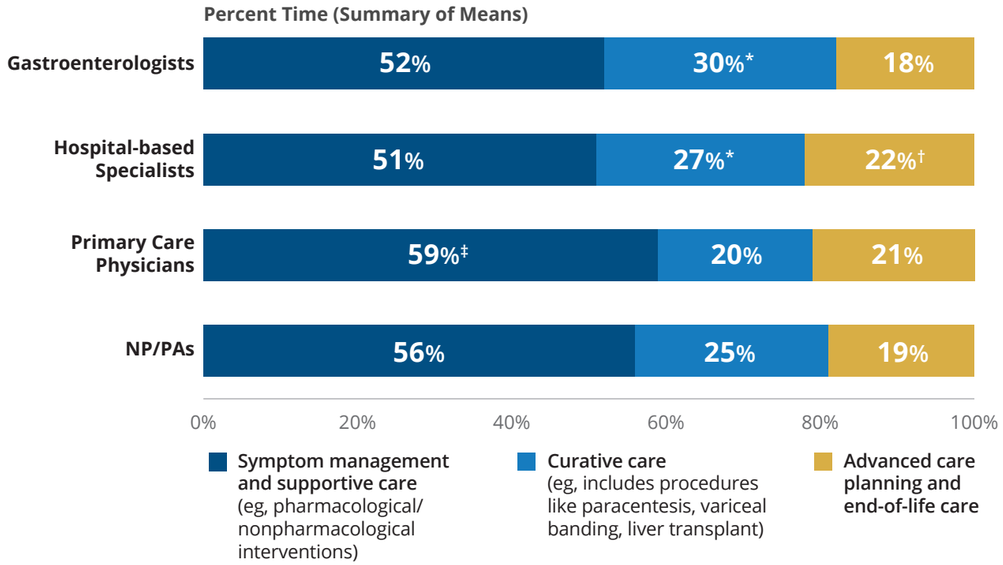
PRIMARY MARKET RESEARCH

Provider management focus for patients with cirrhosis is captured in Figure 22.

With respect to patients with cirrhosis, approximately 50% of specialist time (gastroenterologist and hospital-based specialists) is spent on symptom management and supportive care, approximately 30% on curative interventions, and the remaining time on palliative care and end-of-life planning.

Figure 22 | **Provider Management Focus for Cirrhotic Patients**

Q3.9. Of the cirrhotic patients that are currently in your practice, how much time do you spend on the following 3 areas of care management?



N=400 (100 Gastroenterologists, 100 Hospital-based Specialists, 100 PCPs, 100 NPs/PAs).
*This number is statistically significant at 95% confidence versus PCPs.
†This number is statistically significant at 95% confidence versus Gastroenterologists.
‡This number is statistically significant at 95% confidence versus Hospital-based Specialists and Gastroenterologists.

Note: The market research and statistical analysis in this report were conducted in a manner consistent with industry standards and market research codes of conduct; however, this is in no way comparable to the scientific rigor of clinical research. All statistical significance in this report is at 95% confidence.

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Figure 23 summarizes NPs/PAs and PCPs' management and referral patterns for HE patients by grade (West Haven Criteria).

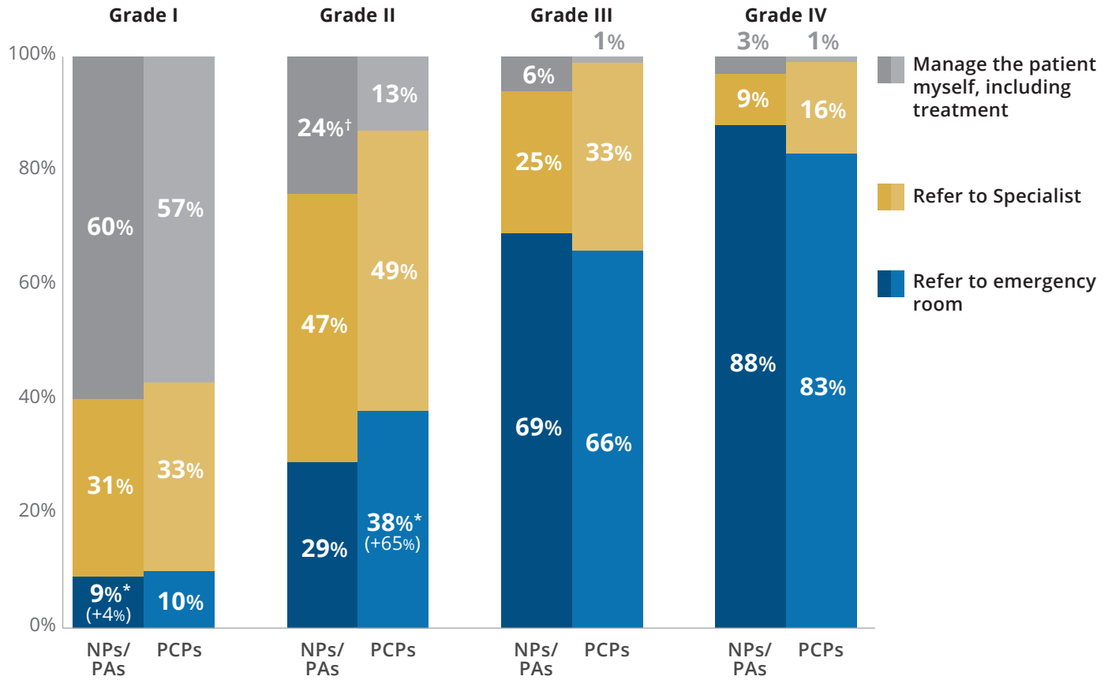
The majority of Grade I patients are managed by PCPs and NPs/PAs (60% and 57%, respectively) with patient referrals incrementally increasing for Grades II through IV. They refer the majority of Grade III/IV patients to the emergency department.

This year, it was noted that NPs/PAs were sending statistically significantly more Grade I patients (+4%) and PCPs were sending more Grade II patients (+65%) to the emergency room versus the previous years (at 95% confidence).

Please see the Methodology (page 10 of this report) Limitations of Market Research and Statistical Analysis section.

Figure 23 | **Provider Management for Hepatic Encephalopathy (Grade I to IV)**

Q32. What is your approach to managing patients with hepatic encephalopathy (HE) by Grade I to IV?



N=200 (100 PCPs, 100 NPs/PAs).
*This number is statistically significant (at 95% confidence) versus last year.
†This number is statistically significant (at 95% confidence) versus PCPs.
Values in parentheses indicate percent change versus 2022.

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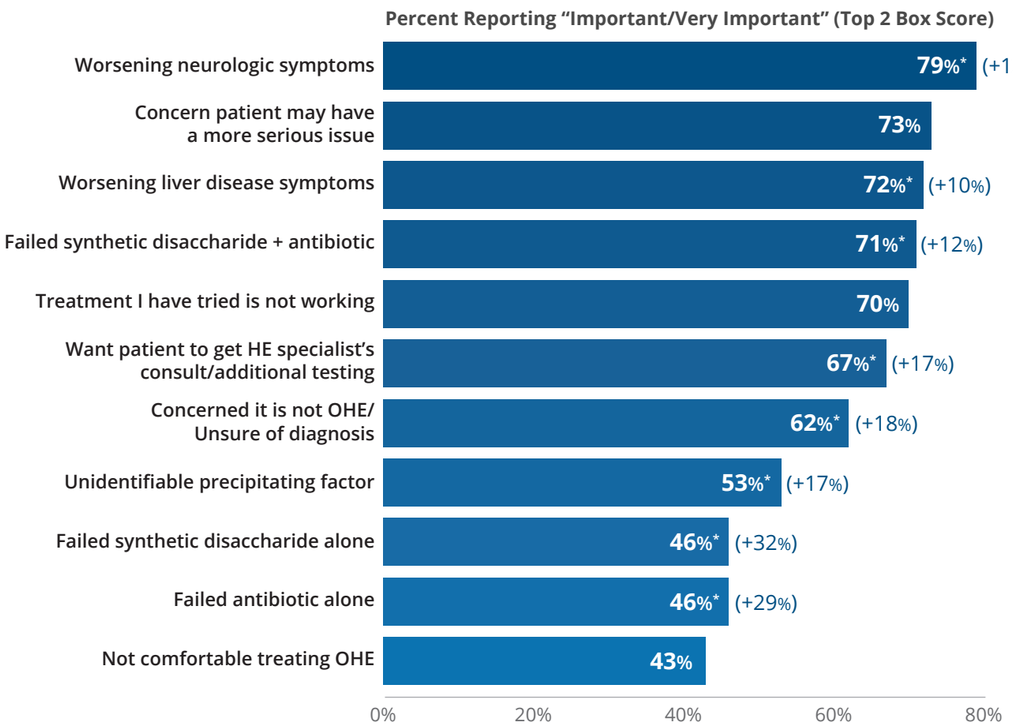
Figure 24 shows the importance ratings for factors that determine a decision for a referral and/or consult for a patient who has overt hepatic encephalopathy (OHE).

79% of respondents rated worsening neurologic symptoms as the most important factor that prompts the decision to seek a referral or consult for OHE. This factor increased 12% versus 2022 (at 95% confidence) and was a result of higher importance ratings this year by the hospital-based specialists and NPs/PAs.

Figure 24 | **Factors Important in Determining Decision to Get a Referral or Consult for OHE**

Q37. Please rate the importance of the following factors in determining your decision to get a referral or consult for a patient who has overt hepatic encephalopathy (OHE). Please use a 7-point scale, where 1=not at all important and 7=very important.



N=400 (100 Gastroenterologists, 100 Hospital-based Specialists, 100 PCPs, 100 NPs/PAs).
*This number is statistically significant at 95% confidence versus last year.
Values in parentheses indicate percent change from 2022.

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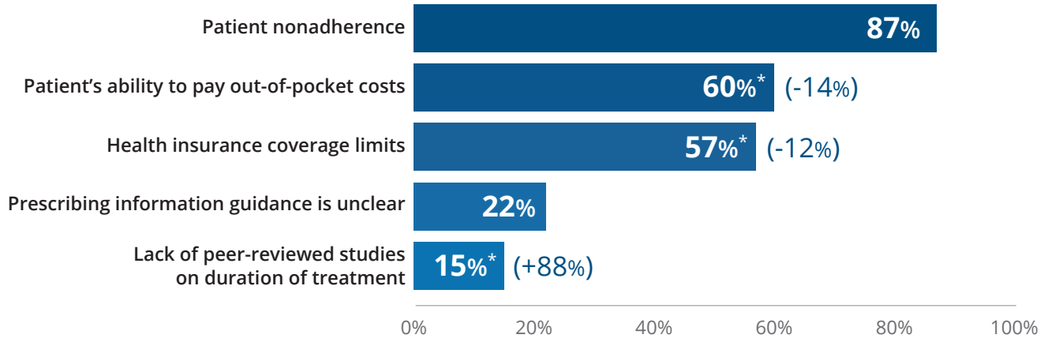
Figure 25 shows the factors that most commonly limit the duration of treatment for the prevention of HE recurrence.

While the vast majority of respondents (89%) recognize that the duration of treatment for HE is indefinite, many factors can interfere, causing interruptions in therapy and/or recurrent OHE.

87% of respondents cite patient nonadherence as the most common factor that limits the duration of treatment to prevent HE recurrence.

Figure 25 | **Factors That Most Commonly Limit Duration of Treatment for the Prevention of OHE Recurrence**

Q58. What factors most commonly limit the duration of treatment for the prevention of hepatic encephalopathy (HE) recurrence? Please select all that apply.



N=400 (100 Gastroenterologists, 100 Hospital-based Specialists, 100 PCPs, 100 NPs/PAs).
*This number is statistically significant at 95% confidence versus last year.
Values in parentheses indicate percent change from 2022.

"It was reassuring to see that more PCPs are sending patients with HE to the ER. This is the first step (of many) to help patients understand the gravity of the condition and start to become connected to appropriate therapy. Still, most grade 1 HE is still managed by nonspecialists (though it is possible the APPs are in GI practices). HE, irrespective of grade, carries a high mortality risk. We need to continue to educate our primary care providers that early recognition and referral will prevent complications.

- But poor adherence continues to be the leading reason HE is not well managed. Much of this is the inability to pay for medications after hospitalization. But providers are not using the appropriate coding, which suggests they are not doing the prior authorization or accurately justifying the reason for the medications."

—Primary care physician

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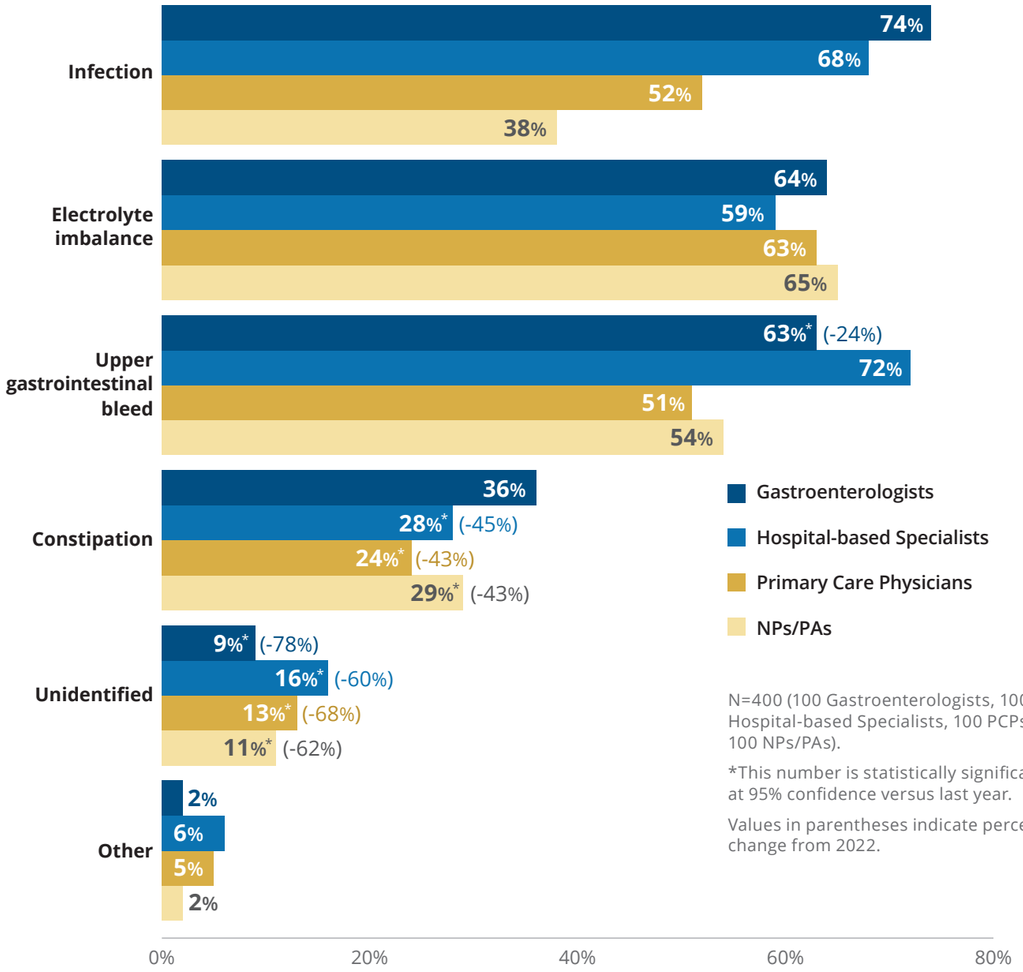
In Figure 26, respondents report on the most common precipitating factors in newly diagnosed OHE.

74% of gastroenterologists report that infections are the most common precipitating factor in their practice setting for those newly diagnosed with HE.

Not surprisingly, 72% of hospital-based specialists see upper bleeds more commonly, whereas 63% of PCPs and 65% of NPs/PAs see electrolyte imbalances.

Figure 26 | **Most Common Precipitating Factors in Newly Diagnosed OHE Patients**

Q35b. Which precipitating factors most commonly present in your newly diagnosed overt hepatic encephalopathy (OHE) patients? Please select all that apply.



N=400 (100 Gastroenterologists, 100 Hospital-based Specialists, 100 PCPs, 100 NPs/PAs).

*This number is statistically significant at 95% confidence versus last year.

Values in parentheses indicate percent change from 2022.

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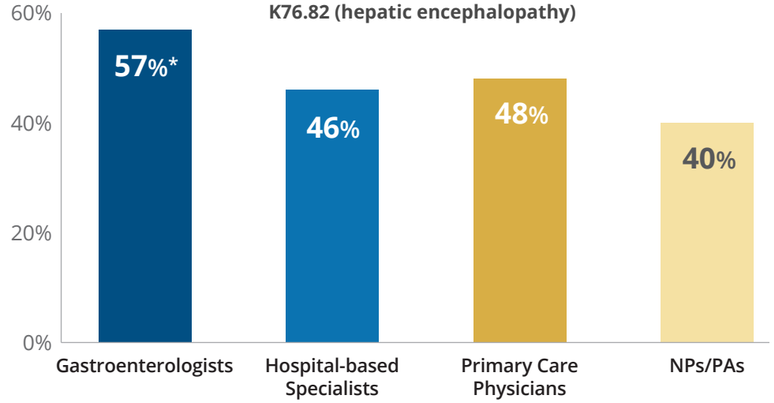
Figure 27 shows respondents' adoption of the dedicated ICD-10 code (K76.82) for HE.

Over 40% of respondents have readily adopted the ICD-10 code (K76.82) for HE.

Figure 27 | **Providers' Adoption of Dedicated ICD-10 Code (K76.82) for the Treatment of Hepatic Encephalopathy**

Q39. Which ICD-10 code do you most commonly use when prescribing lactulose for hepatic encephalopathy (HE)?



N=400 (100 Gastroenterologists, 100 Hospital-based Specialists, 100 PCPs, 100 NPs/PAs).

*This number is statistically significant at 95% confidence versus NPs/PAs.

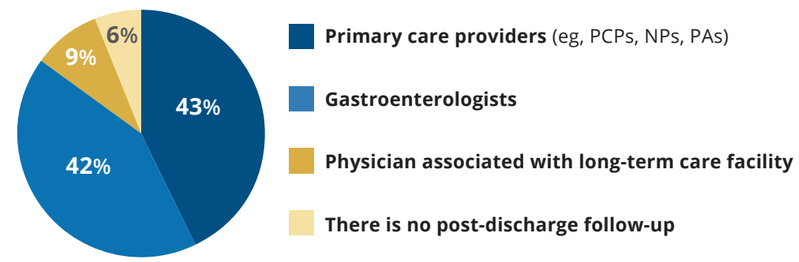
In Figure 28, respondents report on what provider type their patients follow up with after discharge from the hospital for a liver-related condition.

Post hospital discharge, all survey respondents report patients who most commonly have follow-up visits typically see a gastroenterologist or primary care provider.

43% of urban/suburban survey respondents report statistically significant higher patient follow-up visits with gastroenterologists post hospital discharge versus 31% of rural respondents (at 95% confidence).

Figure 28 | **Provider Types Liver Disease Patients Most Commonly See Post Hospital Discharge**

Q55. After being hospitalized for a liver disease–related condition (eg, OHE), what percent of your patients have a scheduled visit with providers for follow-up?



N=400 (100 Gastroenterologists, 100 Hospital-based Specialists, 100 PCPs, 100 NPs/PAs).

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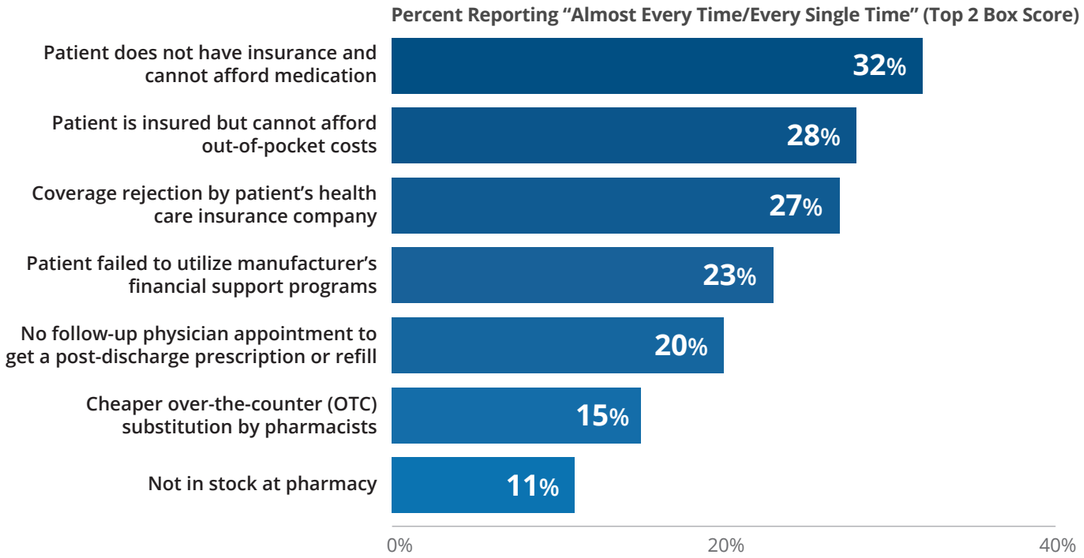
In Figure 29, respondents rated the frequency of cost-related barriers impact on patients' ability to fill prescriptions post discharge from the hospital.

32% of all survey respondents report that the inability to pay for medication post hospital discharge happens the most frequently (almost every time/every single time).

Figure 29 | **Cost-related Barriers Patients Face When Filling Prescriptions Post-discharge**

Q61. How often, if at all, do the following barriers prevent a patient from filling their prescriptions post-discharge from the hospital for a liver disease–related condition? Please use the following 5-point scale, where 1=never and 5=every single time.



N=400 (100 Gastroenterologists, 100 Hospital-based Specialists, 100 PCPs, 100 NPs/PAs).

Evolving Role of PCPs and NPs/PAs

Advanced Practice Providers Can Meet the Challenges of NAFLD Care

SECONDARY RESEARCH FROM PEER-REVIEWED PUBLICATIONS

Optimal NAFLD care demands the ability to deliver effective behavioral interventions in addition to arranging the appropriate referrals (eg, nutrition, bariatrics). These skills, variable among clinicians, require time for patient education.[23]

Devoted to clinical care delivery and trained in a tradition focused on patient-centered education, APPs (NPs and PAs who assess patients, order and interpret diagnostic testing and labs, and formulate treatment plans) may be best suited to meeting the challenges of NAFLD care.[23]

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The value in the patient's first visit for NAFLD is derived from the effect it has on them and, therefore, the quality of the education they receive. APPs have the greatest impact here. The clinician's task is to efficiently explain the condition and effectively connect with the patient on their level in a way that encourages lifestyle change.[23]

Using a retrospective analysis of a nationally representative American commercial claims database (Optum) from 2001 to 2015 which included 389,257 unique adults with cirrhosis, compared cirrhosis patients without APP (N=222,549)—defined as NPs or PAs—care, patients with APP care (N=166,708)[21]:

- Higher rates of hepatocellular carcinoma screening (adjusted odds ratio [OR]: 1.23; 95% CI: 1.19, 1.27)
- Higher rates of varices screening (OR: 1.20; 95% CI: 1.13, 1.27)
- Higher use of gut-specific antibiotic after a discharge for OHE (OR: 2.09; 95% CI: 1.80, 2.43)
- Reduced risk of 30-day readmission (OR: 0.68; 95% CI: 0.66, 0.70)
- Patients with cirrhosis under the care of an APP had a reduced risk of death (adjusted HR: 0.57; 95% CI: 0.55, 0.60)

A separate large national comparison between APPs and physicians on the use of low-value health services revealed that APPs and physicians in both office- and hospital-based primary care settings provided equivalent amounts of low-value care, including antibiotics, scans, and referrals to other physicians.[24]

The information above points to the potential need to increase the role of PCPs, NPs, and PAs to identify and manage CLD/cirrhosis and its complications due to the continuing shortage of gastroenterologists.

PRIMARY MARKET RESEARCH

Figure 30 asks gastroenterologists and PCPs to report on the provider type that they feel is best equipped to manage and follow NASH and NAFLD patients as well as the comorbidities associated with liver disease.

"There's some mid-levels that are very, very good at what they do, and there's some that may miss signs that it is time to refer the patient. I think if they're trained properly, and they know the algorithms and what to look for, it can help with managing early-stage disease."

—Gastroenterologist

"I do think that NASH is likely to follow the Hep C model—where we've seen a transition over time from specialist to PCP. For that to happen, diagnosis will need to become easier using validated noninvasive tests rather than liver biopsies alongside more FDA-approved treatments. But, you know, if a PCP is seeing a patient every seven minutes, it's going to be hard to delve into NASH."

—Gastroenterologist

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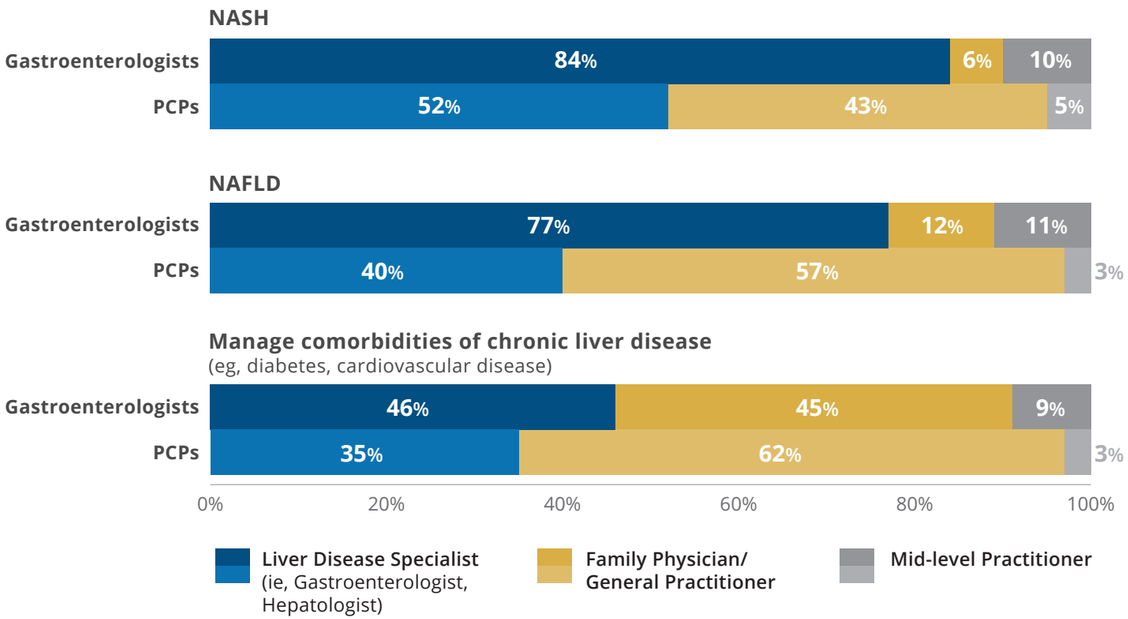
Gastroenterologists and PCPs do not agree on who is best equipped to manage NAFLD:

- 77% of gastroenterologists report that a liver disease specialist is the best provider.
- 57% of PCPs believe that family physicians/general practitioners are the most appropriate provider.

Figure 30 | **Providers' Perceptions on Ideal Provider to Manage Early-stage Liver Disease**

Q52a. Based on your personal experience, which provider type is best equipped to manage and follow (for disease progression) the following liver disease patients?



N=200 (100 Gastroenterologists, 100 PCPs).

"In our clinic we get a lot of referrals from PCPs when their patient gets an ultrasound and it says fatty liver. I'm not sure if that's the right practice, and I think we're trying to change that because I think primary care providers should be dealing with early stages of NAFLD and NASH."

—Gastroenterologist

"Using mid-level practitioners is positive in a sense that it allows for better accessibility, decreased wait times; but I worry that it may lead to decreased patient satisfaction scores given that they're not seeing a physician and then I get worried about fundamental knowledge that some of these mid-level providers have."

—Rural internist

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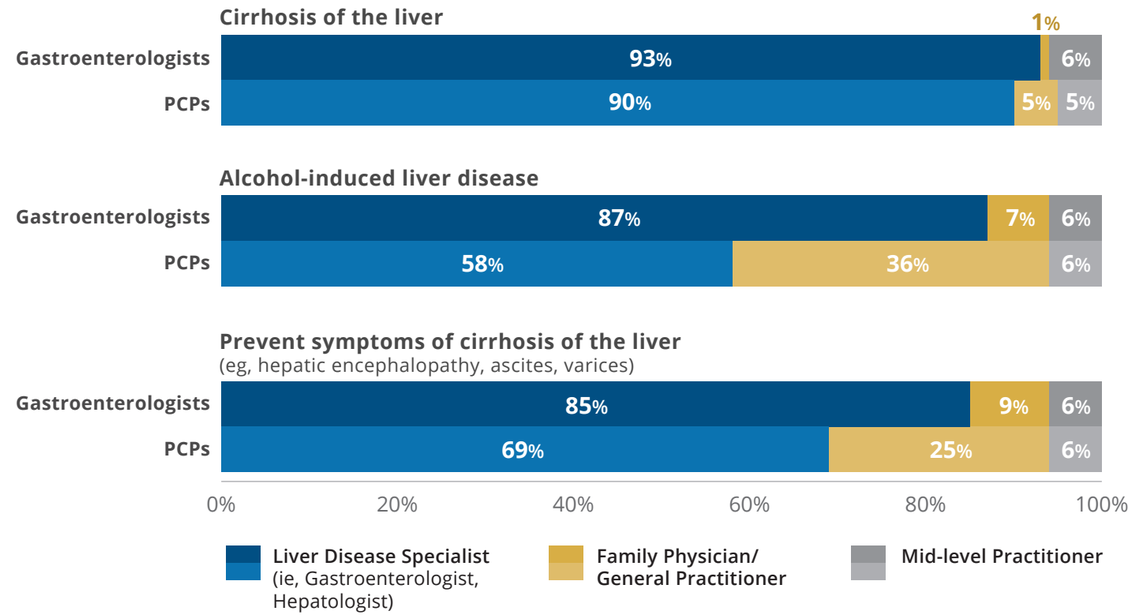
Figure 31 asks gastroenterologists and PCPs to report on the provider type that they feel is best equipped to manage and follow more complex liver disease patients (eg, alcohol-associated liver disease) as well as preventing the complications (symptoms) of cirrhosis (eg, ascites, HE).

≥85% of gastroenterologists feel that the specialist (hepatologist and/or gastroenterologist) is best equipped to manage patients with advancing liver disease.

PCPs agree that overall, specialists are best suited to manage this advanced patient population but see a role for themselves managing alcohol-related liver disease and in preventing symptoms of cirrhosis.

Figure 31 | **Providers' Perceptions on Ideal Provider to Manage Advanced Liver Disease**

Q52b. Based on your personal experience, which provider type is best equipped to manage (and follow for disease progression) the following liver disease patients?



N=200 (100 Gastroenterologists, 100 PCPs).

"There is a lot of specialization that goes on within primary care practices when you start seeing a lot of one patient type—for example, reproductive health. I don't think that happens as much for liver disease—unless you're seeing patients living with HIV or substance abuse."

—Primary care physician

"Our part of the country utilizes a lot of these traveling nursing contracts, so while we have ample nurses, they may not have the depth of knowledge of the system or limitations as what someone may have if they were in our system for a prolonged period of time."

—Rural internist

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Patient Engagement

PRIMARY MARKET RESEARCH

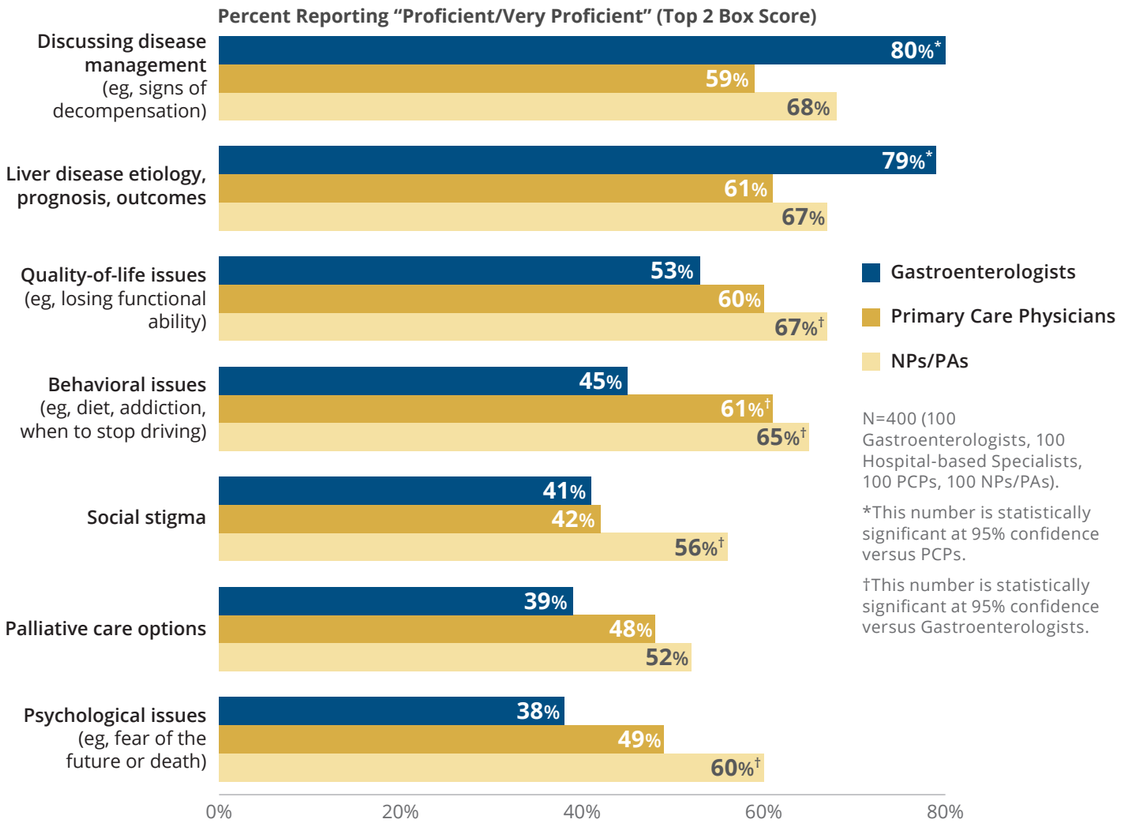
In Figure 32, providers rate themselves on their proficiency discussing various topics with liver disease patients.

Gastroenterologists report the highest degree of proficiency when engaging liver disease patients on the topics of liver disease etiology, outcomes, prognosis, and management (all statistically significant versus PCPs). Conversely, PCPs and NPs/PAs feel more proficient versus the gastroenterologists in discussing quality of life, behavioral and psychological issues, social stigma, and palliative care options.

Please see the Methodology (page 10 of this report) Limitations of Market Research and Statistical Analysis section.

Figure 32 | **Self-reported Proficiency in Communicating With Patients**

Q3.31. When thinking about your interactions with patients living with liver disease, how proficient are you discussing the following topics? Please use a 1 to 7 scale, where 1=not at all proficient and 7=extremely proficient.



N=400 (100 Gastroenterologists, 100 Hospital-based Specialists, 100 PCPs, 100 NPs/PAs).

*This number is statistically significant at 95% confidence versus PCPs.

†This number is statistically significant at 95% confidence versus Gastroenterologists.

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"At stage III cirrhosis, we talk about the complications and what can be done. It's important to have these conversations at the time of diagnosis and that it is documented in their chart. I think unfortunately we have some of these conversations too late, so the patients are coming in, for example during COVID and we're having all these end-of-life decisions."

—Primary care physician

"When engaging patients, in our EHR or in our patient visit summaries we only ever refer to NASH as NASH or hepatic steatosis. It may be a small thing, but it makes a big difference to patients—if they see or hear fatty liver disease beside obesity, it's just a lot for them to handle. It is unnecessary."

—Primary care physician

Figure 33 expresses the degree of provider agreement with the various statements that pertain to patients living with liver disease.

≥55% of respondents indicated strong agreement with the need for:

- Better tools to help them access current and future care needs (59%)
- Addressing unmet patient information needs to help improve patient engagement in care management and reduce anxiety (56%)
- Earlier integration of palliative care and community services (55%)

"It does feel like there's a lot of work to be done with patients around [early-stage] liver disease, education, and teaching people what this means—that it's reversible and the liver is the only organ really that can heal."

—Primary care physician

"We need more patient-friendly literature, patient-friendly materials that help people understand what the underlying pathology is and how integral patient's role is as it pertains to being active participants."

—Nurse practitioner

"I think the stigma can prevent patients from talking about their liver disease—it is embarrassing for them. I do not think that it's very widely known that you can have liver disease outside of alcoholism."

—Primary care physician

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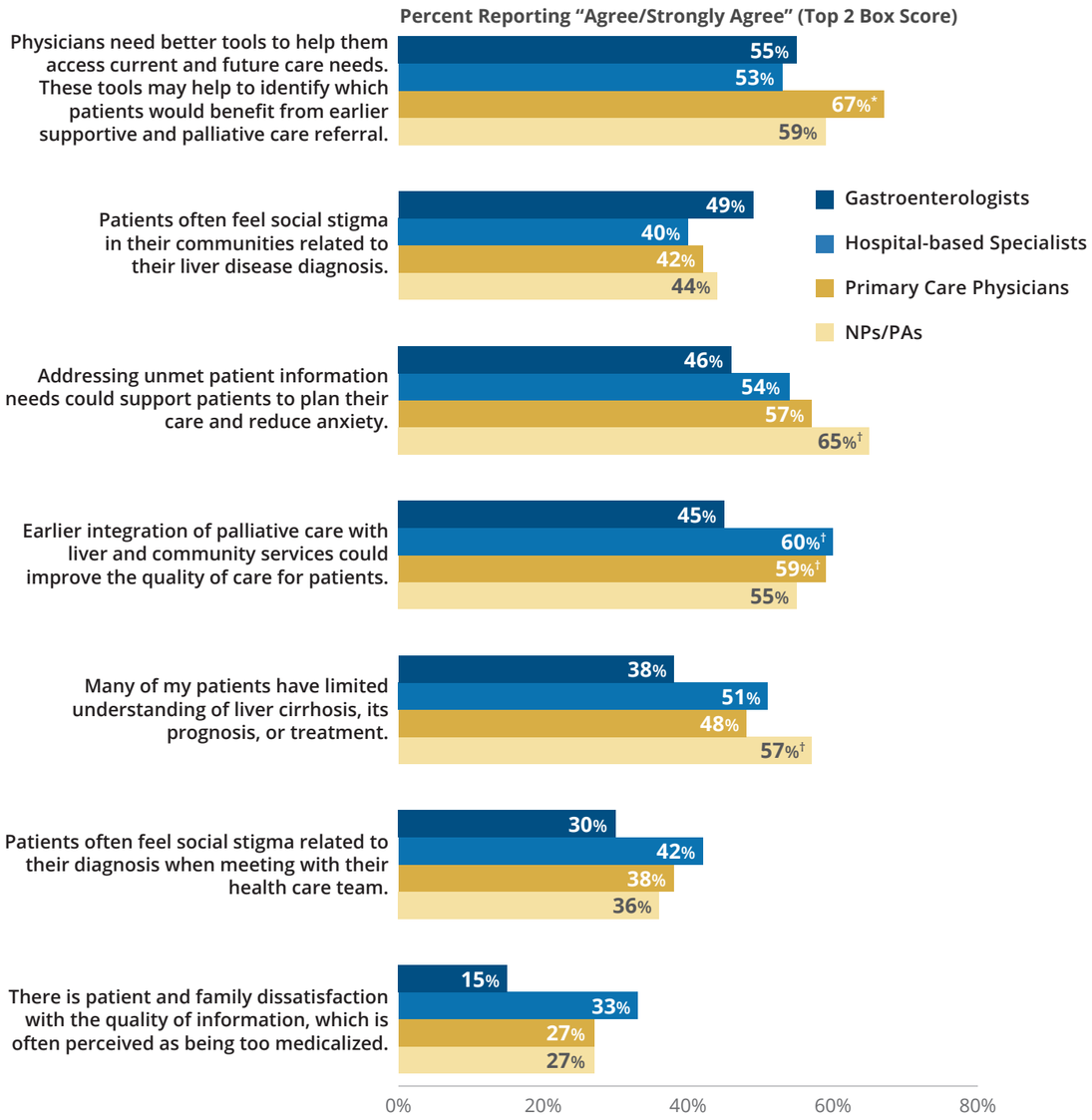
Figure 33 | **Respondent Agreement on Liver Disease Patients' Unmet Needs**

Q3.30. Please indicate your agreement with the following statements as each pertains to your patients who are living with advanced liver disease. Please use a 7-point scale, where 1=do not agree at all and 7=strongly agree.



N=400 (100 Gastroenterologists, 100 Hospital-based Specialists, 100 PCPs, 100 NPs/PAs).
*This number is statistically significant at 95% confidence versus Hospital-based Specialists.
†This number is statistically significant at 95% confidence versus Gastroenterologists.

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Patient Perspectives on the Stigma Associated With Chronic Liver Disease

KEY FINDINGS FROM SECONDARY RESEARCH FROM PEER-REVIEWED PUBLICATIONS

According to a 2014 survey of 149 patients with cirrhosis, regardless of etiology, patients with liver disease experience stigmatization, which negatively affects patients' quality of life. Stigmatization in patients with liver disease is associated with depression, a lack of social support, and a decrease in the tendency to seek health care.[25]

Health care professionals need to be aware of these perceptions and their impact on patients' interaction with the health care system and should consider addressing stigmatization when counseling patients.[25]

A mixed-method systematic review that summarized findings from 95 studies from January 2000 to October 2020 in 26 countries and included over 37,000 patients states that the self-reported causes of impaired quality of life (apart from the symptoms of liver disease) include[26]:

- Unmet needs for information
- Education
- Support from families and health care professionals
- Increased public awareness with a focus on destigmatization

How can we improve patients' quality of life?[26]

21,116 with chronic hepatitis B and C

7264 with nonalcoholic fatty liver disease

4971 with autoimmune or cholestatic liver disease

2696 with liver cirrhosis of different etiologies

1254 with hepatocellular carcinoma

>37,000 patients say we need to focus on:

- **Better education and information**
- **Psychosocial support**
- **Public destigmatization**

Mixed-method systematic review of 95 studies from 26 countries

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Types of Stigma

There are 3 distinct types of stigma: structural, public, and self.

Structural stigma is prejudice and discrimination by policies, laws, and constitutional practice. Examples include discrimination in housing, employment opportunities, restrictions for jury duty, political office, parental custody, marriage, and disparities in treatment.[27]

Public stigma is stereotypes, prejudice, and discrimination endorsed by the general public. Examples include negative stereotypes, attitudes, beliefs, and behaviors about mental illness, persons with mental illness, and their families and providers; isolation and rejection of these groups; lack of public support for services; and support for coercive practices.[27]

Self-stigma occurs when a person internalizes the perceived stigma and applies it to him or herself. The effect of self-stigma includes lowered self-esteem, decreased self-efficacy, and psychologically harmful feelings of embarrassment and shame.[27]

What Patients Want From the Medical Community

KEY FINDINGS FROM PRIMARY MARKET RESEARCH

Patients are hopeful that the medical community (eg, providers, health systems, providers' professional organizations, and health insurance companies) will act as advocates to people living with liver disease and address the personal and structural stigma that exists that prevents early disease detection and optimal disease state management.

This would include:

- Developing and adopting best-practice guidelines for screening for various liver diseases (including diagnostic tests) to ensure early detection
- Providing a comprehensive understanding of the potential disease trajectory at time of diagnosis (eg, that a diagnosis of early-stage liver disease can eventually lead to end-stage liver disease [cirrhosis], cancer, and transplant). Give patients the directive and support to learn everything they can about their disease, seek resources, join advocacy groups, engage in treatment, and provide the necessary follow-up.
- Providing comprehensive patient education materials and/or resources at time of diagnosis (eg, links to patient advocacy groups)
- Encouraging people living with liver disease to engage in their disease management: seeking psychosocial support (via their family, friends, or support groups) and learning everything they can about their disease (online advocacy groups, Facebook groups, local community groups). Ideally, give them links to these valuable resources (see Appendix).
- In the absence of curative treatment, addressing and managing with regular follow-up the comorbidities associated with liver disease that can impact patients' quality of life, ability to engage in their disease management, and/or acceleration of their disease (eg, obesity, alcohol consumption, depression, fatigue)

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- Patients living with liver disease recognizing the complexity of their disease state and the need for multidisciplinary care providers. They are looking for comprehensive care that can meet the needs of the individual and address disparities in care that exist (eg, access to primary care providers, liver specialists, diagnostic tests, social workers, dietitians, treatments, etc).
- Recognition of our shared humanity—people living with liver disease ask providers to consider their own personal biases (or knowledge gaps) toward patients living with liver disease and use this knowledge to improve patient engagement and management practices. Increase awareness and understanding of other socioeconomic factors that contribute to liver disease (race, class, trauma history).
- Choice of language, which is important in addressing stigma, building trust, and improving patient engagement in disease management
- Listening to patients and liver disease patient advocacy organizations—patients' lived experiences matter, and they have important information to share with you. Look to partner with advocacy organizations to best understand universal patient needs (eg, the need for the development).
- Providers, and health systems specifically, reducing societal and structural stigma as well as demanding better coverage for their liver disease patient population from health care providers:
  - Educate widely on the importance of liver health and the impact of liver disease.
  - Encourage professional provider organizations to develop continuing education programs and updated evidence-based guidelines for all liver disease.
  - Work to standardize care within your larger health care system (eg, update guidelines and patient information links to the electronic health record [EHR] system).
  - Lobby health insurance companies to ensure coverage is aligned with best-practice guidelines (send them best-practice guidelines, fill out prior authorizations, challenge appeals).

Methodology

The goal of the primary research arm was to speak with patients/patient advocates who are living with various types of liver disease to better understand the types of stigma that patients living with liver disease experience. For the purposes of our report, we have defined stigma as any negative attitude, prejudice, or false beliefs directed at individuals living with liver disease. Stigmatization in patients with liver disease is associated with depression, a lack of social support, and a decrease in the tendency to seek health care and/or engage with disease management.[25]

We surveyed the impact of stigma on people living with liver disease and how the medical community (eg, providers, health systems, providers' professional organizations, and health insurance companies) might better support people living with liver disease as it pertains to the stigma they may experience.

Six patient advocates living with various types of liver disease participated in 40-minute telephone interviews. All of the participants also play an active role advocating for individuals living with liver disease. The types of liver diseases discussed included alcohol-associated liver disease, hepatitis B and C, nonalcoholic steatohepatitis (NASH), nonalcoholic fatty liver disease (NAFLD), cirrhosis, liver cancer, and end-stage liver disease requiring transplant.

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Secondary research was conducted utilizing Google and PubMed searches to identify relevant peer-reviewed publications and sources as noted in the report. Secondary research may not reflect all published data. A systematic review was not performed.

What Is Stigma, and Why Does It Matter?

PRIMARY MARKET RESEARCH

In interviews with patient advocates living with liver disease, we defined stigma as any negative attitude, prejudice, or false beliefs directed at individuals living with liver disease. Negative connotations connected to the liver are a well-understood phenomenon in the patient advocacy community.

"We hear a lot [in our support groups] that once a liver issue has been discovered, the doctor says, "Well, you must be drinking. You're not telling me the truth.' We hear that a lot. That assumption is deeply embedded in the human brain that it's alcohol." —Patient/Patient advocate

"We've got one liver, we've got one brain, and we've got one heart. You never hear public service announcements on the liver. Nobody talks about the liver; it's like, 'Eww, the liver.' If we could lower the stigma of the disease, I think we could get more people who would be willing to do live liver transplants." —Patient/Patient advocate

"Our local hospital where I got the transplant has a community event every year where they talk about their transplant activities, and they always focus on the heart. Well, they do many more liver transplants than they do heart transplants. It's like they didn't want to talk about the liver. And I think it all comes back to the stigma; people think you're doing it for alcoholics." —Patient/Patient advocate

Patient advocates would like to see liver disease prevention and disease state management centered by the medical community (eg, providers, health systems, providers' professional organizations, and health insurance companies and legislators).

"Early next month, they have a Capitol Hill Day where we go and talk to legislators about liver disease. Our goal is to get liver disease on the map when they're talking about health problems in this country. I mean, it's widespread, but we just don't hear much about it. We talk to legislators, and they kind of all nod their heads, but nothing seems to get done." —Patient/Patient advocate

Patient interviews confirmed the findings from clinical studies that stigma impacts liver disease patients' quality of life, ability to seek and advocate for care, and ultimately, disease state outcomes.

"Stigma can get in the way of early detection. People are afraid to come forward. Afraid of being called alcoholics. They are afraid of losing their jobs, losing their children, losing basically the life they have if they actually admit to the amount of alcohol they drink. Often, people are not diagnosed until very late stages of their [alcohol-associated] liver disease, and that's why the mortality rates are so high." —Patient/Patient advocate

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Large disparities in care, education, and patient resources exist, especially between liver disease centers of excellence as compared to other practices.

"There are so many wonderful teaching and research hospitals. If you go to one of those, you're going to get really great care. Outside of that there is a lot more stigma because they haven't learned, the language hasn't changed, and the information is not there. I don't think that they understand all the different ways you can detect liver disease. And insurance companies need to really show they'll approve those tests." —Patient/Patient advocate

"I have to battle with my GP [general practitioner] to fill out the pre-authorization forms my insurance carrier requires. I've had to battle them [the insurance company] for 3 to 4 months to get something approved. The typical person I don't think is going to be able to do that all the time." —Patient/Patient advocate

"I think when a lot of these doctors went to medical school, they were taught that fatty liver is a benign disease and it's only been in recent years that people are starting to understand the potential consequences. I know my own PCP, when I went back to him after my transplant, he said he had learned a lesson with me about what can happen [when fatty liver disease goes unmanaged]; and he had become much more aggressive in counseling patients who had fatty liver." —Patient/Patient advocate

What Do Patients Want From the Medical Community?

Patients are hopeful that the medical community (eg, providers, health systems, providers' professional organizations, and insurance companies) will act as advocates to people living with liver disease and address the personal and structural stigma that exists that prevents early disease detection and optimal disease state management.

This would include:

Developing and adopting best-practice guidelines for screening to ensure early detection of all liver diseases

"After people are diagnosed [with NASH, NAFLD], it's a fight with insurance companies and a fight with medical places to get any answers. Providers don't know which is the right [diagnostic test], which one is the gold standard [liver biopsy, MRI, endoscopies, FibroScan]. It is very hard to understand what are the true next steps, and people want reassurance that they are on the right track." —Patient/Patient advocate

"Many providers, as part of your wellness check for new patients, do screening of infectious diseases. They don't ask any questions. They just do a Hep A, B, C, HIV; it's baseline and that's it. That saves time, it's comprehensive, and the patient gets good care that way." —Patient/Patient advocate

"Providers need to recognize that stigma and fear are barriers that keep patients from honestly reporting on their alcohol use." —Patient/Patient advocate

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Providing patients with a clear explanation (roadmap) of the potential disease trajectory at the time of a patient's diagnosis (eg, that a diagnosis of early-stage liver disease may lead to end-stage liver disease [cirrhosis], cancer, and transplant). Patient advocates believe that patients deserve to be informed and empowered.

"You hear it all the time: New members join our group, and it was too late by the time they got their diagnosis [of end-stage liver disease]. No provider ever had the conversation with them. The reoccurring conversation is always like, 'Why wasn't I told this sooner?'" —Patient/Patient advocate

"Health literacy varies from person to person. A diagnosis of cirrhosis doesn't scare people because they don't understand what it means. They understand what cancer means. Providers need to tell people with early liver disease that there's a possibility you could get liver cancer or die from liver failure. And people need to understand that the mortality rate is very high once you get to that point. We need to give them the disease trajectory, we need to give them the tools, and we need to give them the follow-up that's necessary to ensure that they are engaged in their care plan." —Patient/Patient advocate

"When I was diagnosed with fatty liver and they said it's from alcohol, they said, 'So, if you slow down on your drinking, your liver should regenerate, and you should be just fine.'" —Patient/Patient advocate

Providing comprehensive patient education materials and/or resources at time of diagnosis (eg, links to patient advocacy groups)

"After diagnosis [cirrhosis and liver cancer], I did some research online and found a survey that showed that one-third of Americans think you can live without a liver. I felt like my life had been saved by the liver transplant, and I felt like I had an obligation to help others to not follow in my footsteps. We want to educate people that don't know about the disease or those who are in the early stages, who were just diagnosed like I was, and told not to worry about and have no idea what the potential consequences might be." —Patient/Patient advocate

"And there are obstacles—I've had situations where a doctor wants to use a resource we've created [advocacy organization] but they can't get clearance. So, there's some of those bureaucratic obstacles as well. There are patient education materials and websites out there that have useful information. I don't think they've done a good job in making people aware of those resources." —Patient/Patient advocate

Encouraging patients to engage in their disease management: to learn everything they can about their disease and to seek emotional support beyond family and friends (eg, peer-to-peer support [online advocacy groups, Facebook groups, local community groups]). Ideally, give them links to these valuable resources.

"Patient support groups are important. Finding people like you, right, that are suffering from the disease as well, which is the big reason I started this organization. Finding connection, finding belonging, finding your unique pathway to health and understanding—you're empowered by that." —Patient/Patient advocate

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In the absence of curative treatment, addressing and managing the comorbidities associated with liver disease that can impact patients' quality of life, ability to engage in their disease management, and/or acceleration of their disease (eg, obesity, alcohol consumption, depression, fatigue)

"Health care providers don't talk to their patients about some of the psychosocial things, which I would say for Hep B and Hep C may actually contribute to more suffering than the actual physical symptoms themselves. So, when we talk about quality of life, this should be a part—in medicine, we should be committed to improving quality of life." —Patient/Patient advocate

"Patient education on nutrition is lacking. Our [advocate group] website focuses on the link between nutrition and liver health. Because of the high incidence in the Hispanic population, we also want our materials to be available in Spanish. We work with a diabetes doctor here who actually has a teaching kitchen in her practice where she shows people how to eat healthier at a lower cost. If you're on the lower end of the economic spectrum and you live in a food desert, this type of information is important." —Patient/Patient advocate

Patients living with liver disease recognizing the complexity of their disease state and the need for multidisciplinary care providers. They are looking for comprehensive care that can meet the needs of the individual and address the disparities in care that exist (eg, access to primary care providers, liver specialists, diagnostic tests, social workers, dietitians, treatments, etc).

"I can tell you the one thing we have asked the White House—and this is the most important thing they can do for everybody [all liver diseases]—is they need to bring the services to the people. So, in other words, in a single day, people get tested [for Hep C], get the results back, and start medication." —Patient/Patient advocate

"I don't think referrals [to other providers or support roles] happen frequently enough. There really should be a team because typically many patients need support for other issues, like diabetes, weight loss, and mental health. That's one of the reasons we formed this support group: When people get this disease, they know so little about it and they think they are alone." —Patient/Patient advocate

Recognition of our shared humanity—people living with liver disease ask providers to consider their own personal biases [or knowledge gaps] toward patients living with liver disease and use this knowledge to improve patient engagement and management practices. Increase awareness and understanding of other socioeconomic factors that contribute to liver disease (race, class).

"Receiving empathy matters—be it a doctor or therapist. Finding those people in the medical community can be hard sometimes. But when you find the right ones that really engage in your care and really believe in you as a person and believe that you are deserving [of care], those are really important people. It helps you find your own sense of agency." —Patient/Patient advocate

"In the US, there are populations that are disproportionately affected [Asian American, Pacific Islanders, and people with African origins]; and the majority of the time, their transmission is through mother/infant. Why not put that at the top of the list in the literature?" —Patient/Patient advocate

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Choice of language, which is important in addressing stigma, building trust, and improving patient engagement in disease management

"Our organization talks about language all the time—I call it having 'cultural competency.' It is important for providers to know who this person is that they are talking to and what community they belong to. It is about respect and building trust." —Patient/Patient advocate

"I believe that some of the good health systems have updated their terminology with respect to stigmatizing language and using best practices in their patient summaries [using alcohol-use disorder and/or alcohol-associated liver disease]. They might even have auto-correct built into their EHR, and if they don't, that would be a good technological improvement." —Patient/Patient advocate

"So, all the prevention messages are more around get vaccinated. But if you are someone infected, carrying it, the message is, there really isn't anything that can be done. Not managing the disease actively, the clinicians are perpetuating the stigma that there is nothing to be done." —Patient/Patient advocate

Listening to patients and liver disease patient advocacy organizations—patients' lived experiences matter, and they have important information to share with you that could change people's lives. Look to partner with advocacy organizations to best understand universal patient needs (eg, the need for the development and adoption of best-practice guidelines, patient education, and resources).

"You hear all these amazing stories of people who have been treated for Hep C, and it's like they have a new lease on life. They feel differently about themselves. They are motivated and ready to tackle other health issues [weight, diabetes]. For Hep B, there is no treatment available unless they have high viral loads and have signs of liver inflammation. We are not at a place where we offer treatment to all patients." —Patient/Patient advocate

Providers and health systems should consider reducing societal and structural stigma as well as demanding better coverage for their liver disease patient population from health care providers:

- Educate widely on the importance of liver health and the impact of liver disease.
- Encourage professional provider organizations to develop continuing education programs and updated evidence-based guidelines for all liver disease.
- Work to standardize care within the larger health care system (eg, update guidelines and patient information links to the EHR system).
- Lobby health insurance companies to ensure coverage is aligned with best-practice guidelines (send them best-practice guidelines, fill out prior authorizations, challenge appeals).

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Resources

Key Findings:

PRIMARY MARKET RESEARCH

Tools in providers' electronic health records (EHRs) to help providers diagnosis and manage disease progression are limited:

- 75% of respondents report that their EHR system does not have the ability to identify patients at risk of nonalcoholic fatty liver disease/nonalcoholic steatohepatitis (NAFLD/NASH) or liver cirrhosis.
- Only 28% of respondents reported that their EHR system contained liver disease guidelines that directed them to the right level of intervention.
- 43% of respondents report comprehensive care models exist for liver disease (eg, order sets, protocols) in their EHR systems. Of note, respondents coming from urban/suburban areas were more likely to have this feature than rural respondents (a statistically significant difference of 46% versus 23%, respectively).
- 53% of respondents report that their EHR system contains liver disease patient education resources.

UpToDate is utilized by 75% of respondents across all specialties as a "real-time" resource to guide patient management decisions for their liver disease patients.

Respondents had statistically significant increases in their importance ratings versus last year for several of their liver disease resources:

+34% Guidelines created by third parties

+72% Liver disease information and resources in the EHR

+40% Liver disease order set or pathway in the EHR system

"Patient resources are also an important tool that clinicians feel they lack. We know that patients will adhere to therapy if they feel the condition is important and the treatment will improve the condition.

- Lack of patient awareness/understanding is especially poor with NAFLD. Despite involving over 25% of the United States, early recognition and understanding of fatty liver disease is poor.[13]
- It is also interesting that both PCPs and subspecialists feel that they are appropriate for patients with early disease.
  - Here the PCPs have the guidelines on their side (even though they are not aware of them!). The 2022 AACE [American Association of Clinical Endocrinologists] guidelines, the AGA [American Gastroenterological Association] clinical care path, and the 2023 AASLD [American Association for the Study of Liver Diseases] fatty liver guidelines all suggest that early NAFLD (without clinically significant fibrosis) is a primary care problem. And we don't have the subspecialty infrastructure (as above) to even care for this massive volume of patients."

—Nancy Reau, MD, expert panelist

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Provider Resources

PRIMARY MARKET RESEARCH

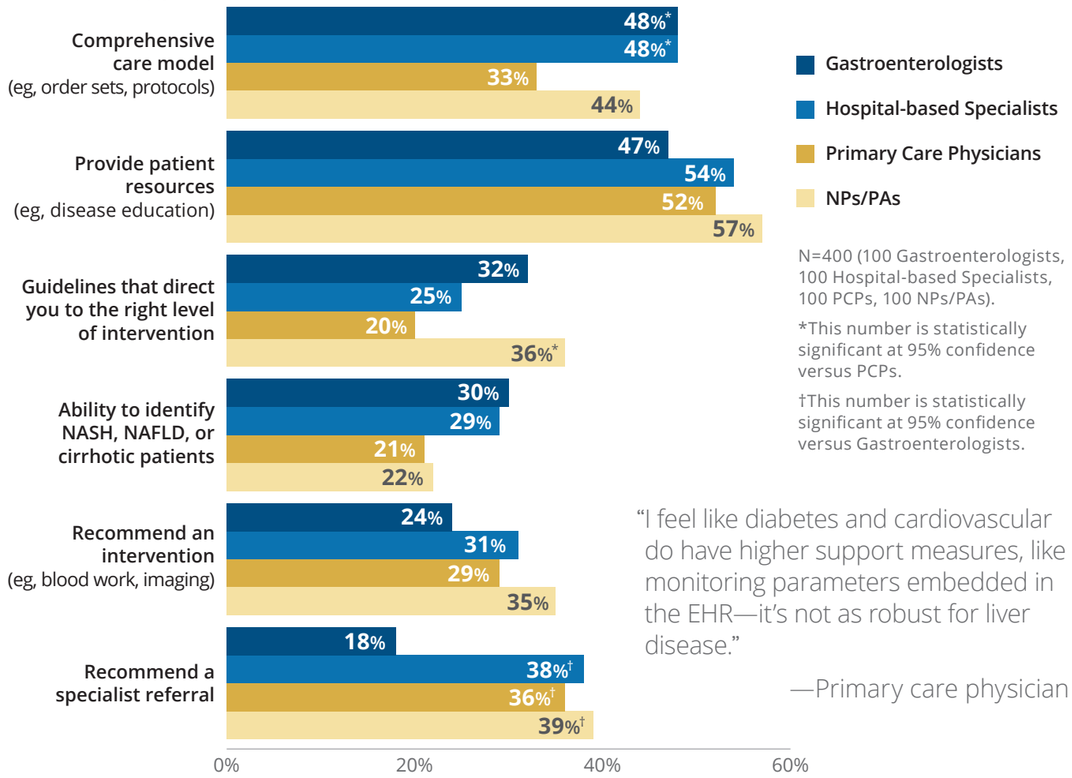
Figure 34 shows the types of information respondents EHR systems might provide that help to guide respondents' management of their liver disease patients.

Tools in providers' EHRs to help providers diagnosis and manage disease progression are limited:

- 75% of respondents report that their EHR system does not have the ability to identify patients at risk of NAFLD/NASH or liver cirrhosis.
- Only 28% of respondents reported that their EHR system contained liver disease guidelines that directed them to the right level of intervention.
- 43% of respondents report comprehensive care models exist for liver disease (eg, order sets, protocols) in their EHR systems. Of note, respondents coming from urban/suburban areas were more likely to have this feature than rural respondents (a statistically significant difference of 46% versus 23%, respectively).
- 53% of respondents report that their EHR system contains liver disease patient education resources.

Figure 34 | **EHR Information That Supports Chronic Liver Disease Patient Management**

Q73. What information does your EHR system provide that helps guide your management of liver disease patients? Please select all that apply.



N=400 (100 Gastroenterologists, 100 Hospital-based Specialists, 100 PCPs, 100 NPs/PAs).

*This number is statistically significant at 95% confidence versus PCPs.

†This number is statistically significant at 95% confidence versus Gastroenterologists.

"I feel like diabetes and cardiovascular do have higher support measures, like monitoring parameters embedded in the EHR—it's not as robust for liver disease."

—Primary care physician

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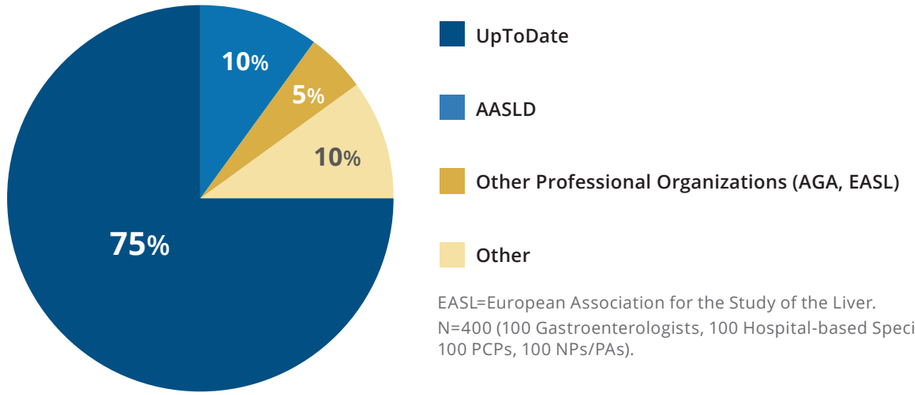
Figure 35 shows provider preference for "real-time" online resources for disease management recommendations.

UpToDate is utilized by 75% of respondents across all specialties as a "real-time" resource to guide patient management decisions for their liver disease patients.

In telephone interviews, providers shared that the online resource they use is often tailored to the question at hand (eg, guidelines versus dosing or side effect management).

Figure 35 | **Providers' Preference for Online Resource to Guide Liver Disease Management**

Q3.7. When you have a liver disease patient sitting in front of you and you need a "real-time" online resource for disease management recommendations, where do you go? Please type in your response.



EASL=European Association for the Study of the Liver.

N=400 (100 Gastroenterologists, 100 Hospital-based Specialists, 100 PCPs, 100 NPs/PAs).

"I think it's pretty common for the larger EHRs to have UpToDate. Ours have several of them, UpToDate, Epocrates, a lot of different ones, but I think UpToDate is probably one of the more common."

—Primary care physician

"UpToDate is an aggregate source for providers to learn about certain subject matters. They have embedded hyperlinks, like guidelines from the American Association for the Study of Liver Diseases, EASL, the NIH [National Institutes of Health]. And, dosing, medication recommendations—it's pretty comprehensive. It is also embedded in our EMR so when you have a patient's chart open—the ease of access is pretty nice."

—Internist

Note: The market research and statistical analysis in this report were conducted in a manner consistent with industry standards and market research codes of conduct; however, this is in no way comparable to the scientific rigor of clinical research. All statistical significance in this report is at 95% confidence.

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In Figure 36, respondents rated the following resources in their ability to support liver disease patient management.

Respondents had statistically significant increases in their importance ratings for several of their liver disease resources:

+34% Guidelines created by third parties

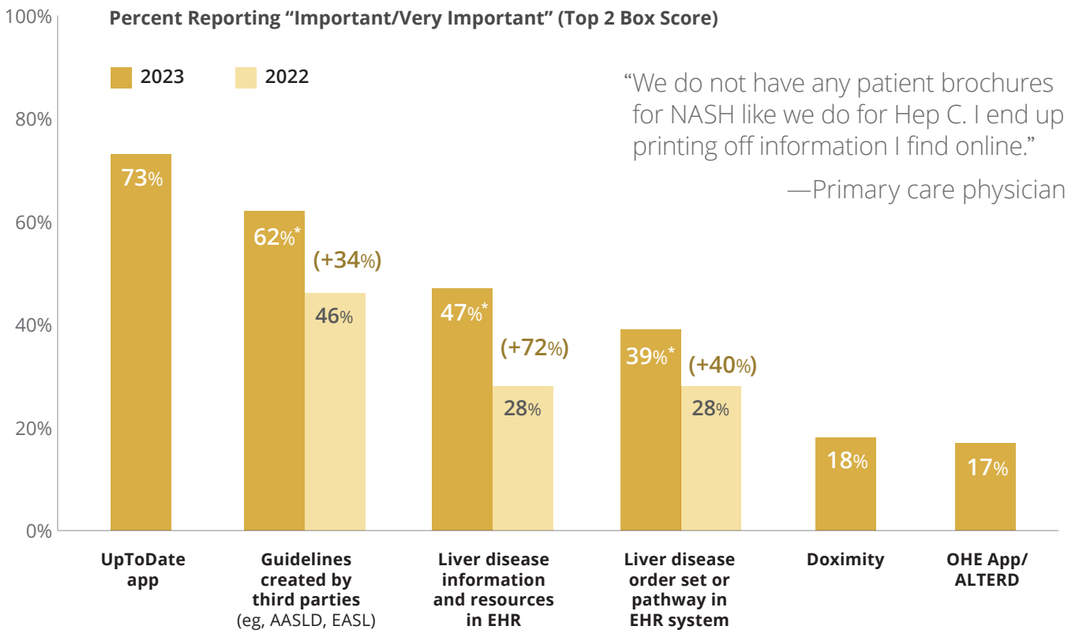
+72% Liver disease information and resources in the EHR

+40% Liver disease order set or pathway in the EHR system

Seventy-three percent of respondents across all specialties rated UpToDate.com as their most important resource supporting liver disease patient management. This was followed closely by guidelines created by third parties, which increased in its importance rating by 34% versus last year.

Figure 36 | **Resources That Support Liver Disease Patient Management**

Q62. Please rate the importance of the following resources in their ability to support liver disease patient management. Please use a 7-point scale, where 1=not at all important and 7=very important.



N=400 (100 Gastroenterologists, 100 Hospital-based Specialists, 100 PCPs, 100 NPs/PAs).
*This number is statistically significant at 95% confidence versus last year.
Values in parentheses indicate percent change from 2022.

"We do not have any patient brochures for NASH like we do for Hep C. I end up printing off information I find online."

—Primary care physician

"I use a NAFLD dietary plan that I put together myself because—there's not a great one [a one-pager]—that's available on our EHR."

—Primary care physician

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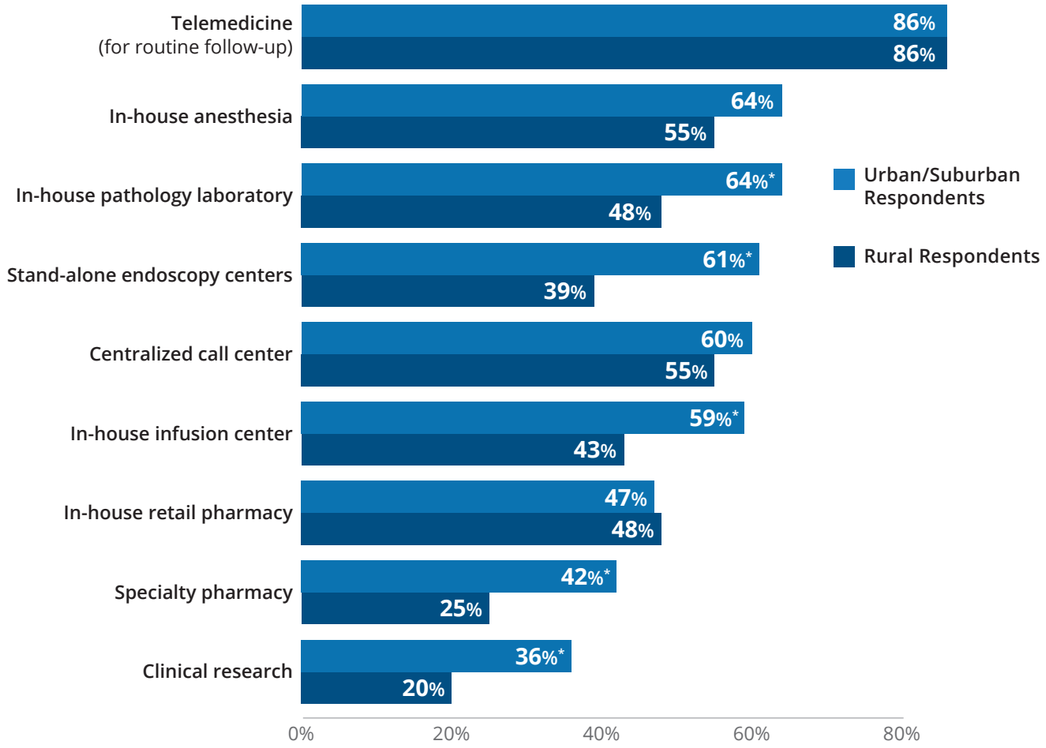
Ancillary Services

Figure 37 shows the percent of respondents located in either urban/suburban or rural locations who have the following ancillary services available at their organization.

Ancillary services are generally less available to respondents in rural settings, and in many cases, statistically significant differences occurred as compared to urban/suburban respondents (ie, fewer in-house pathology labs, stand-alone endoscopy centers, in-house infusion centers, specialty pharmacies, and clinical research).

Figure 37 | **Ancillary Services Available at Urban/Suburban Versus Rural Locations**

Q3.26. Considering all of your organization's sites of care, do your or other sites offer the following ancillary services to patients?



N=400 (356 Suburban/Urban-based Providers, 44 Rural-based Providers).
*This number is statistically significant at 95% confidence versus rural-based providers.

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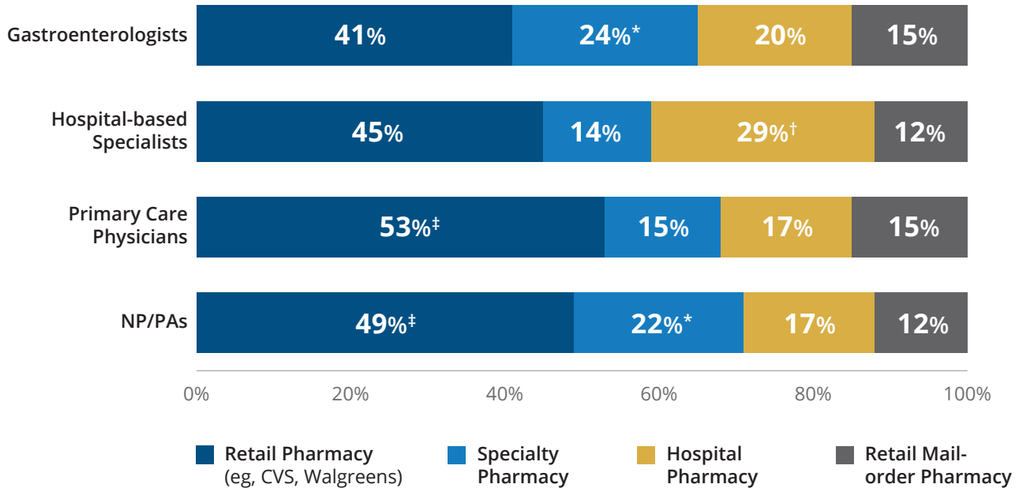
Figure 38 shows the types of pharmacies used by chronic liver disease (CLD) patients.

60% of respondents report their patients with CLD utilize retail pharmacies (including retail mail order).

In telephone interviews, respondents said that in some cases, specialty pharmacy organizations were helpful in minimizing the administrative burden (eg, prior authorizations) or that they hoped their use would translate into a better patient experience.

Figure 38 | **Types of Pharmacies Used by CLD Patients**

Q56. What percent of your prescriptions for chronic liver disease medications are sent to the following locations?



N=400 (100 Gastroenterologists, 100 Hospital-based Specialists, 100 PCPs, 100 NPs/PAs).
*This number is statistically significant at 95% confidence versus Hospital-based Specialists and PCPs.
†This number is statistically significant at 95% confidence versus all others.
‡This number is statistically significant at 95% confidence versus Gastroenterologists.

"We are trying to partner with a specialty pharmacy—we don't have access to that right now. We hope it will provide a better and more personalized patient care experience."

—Internist

"I use specialty pharmacies because most of the insurance companies require prior authorizations for the antiviral agents and they want them handled by specialty pharmacies."

—Internist

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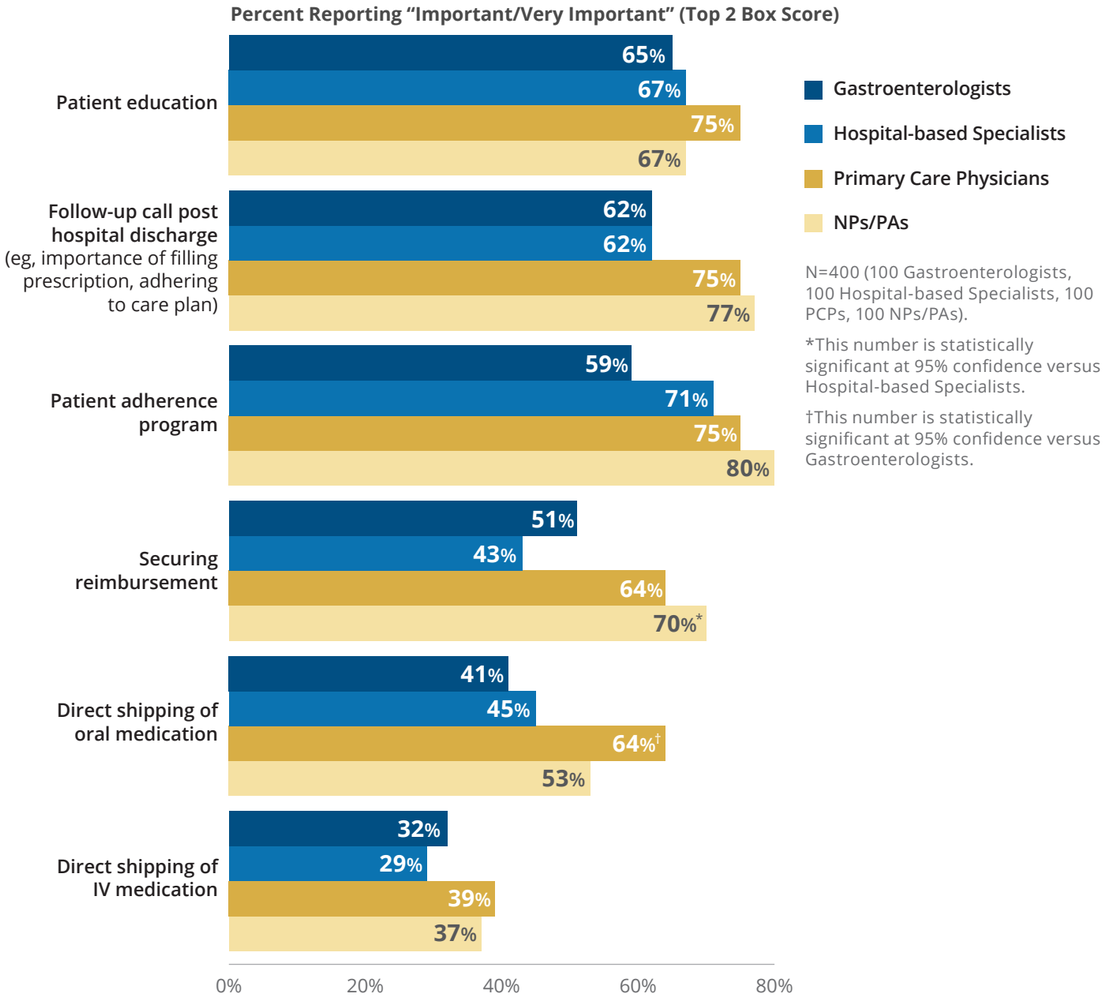
Figure 39 shows the types of services that specialty pharmacies offer that are important in supporting patients living with liver disease.

Collectively, respondents rated patient adherence programs, follow-up calls post hospital discharge, and patient education services as the most important services that specialty pharmacy offers in support of their liver disease patients.

Figure 39 | **Specialty Pharmacy Services That Support Liver Disease Patients**

Q3.27. Of the following services that your specialty pharmacy offers, which do you feel are most important in supporting patients living with liver disease? Please use a 7-point scale, where 1=not at all important and 7=very important.



N=400 (100 Gastroenterologists, 100 Hospital-based Specialists, 100 PCPs, 100 NPs/PAs).

*This number is statistically significant at 95% confidence versus Hospital-based Specialists.

†This number is statistically significant at 95% confidence versus Gastroenterologists.

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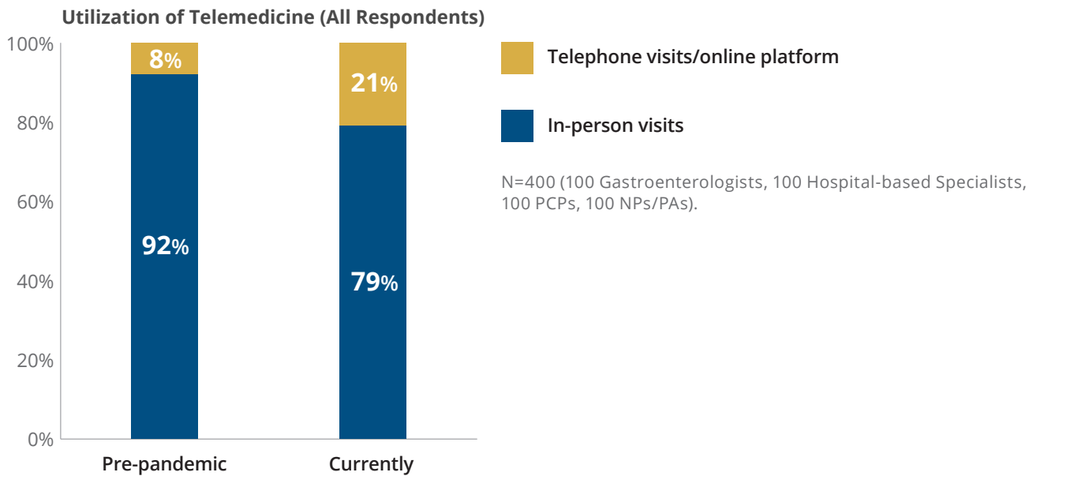
Figure 40 shows that utilization of telemedicine remains higher than pre-pandemic levels (21% versus 8%, respectively).

Utilization of telemedicine remains higher than pre-pandemic levels (21% versus 8%, respectively).

In telephone interviews, respondents stated that the pandemic accelerated their adoption of telemedicine.

Figure 40 | **Utilization of Telemedicine—Pre-pandemic Versus Current Utilization**

Q3.28.1 What percent of all your liver patients' routine office visits (that do not require a physical exam) are delivered by the following means?



N=400 (100 Gastroenterologists, 100 Hospital-based Specialists, 100 PCPs, 100 NPs/PAs).

"The pandemic accelerated the adoption of telemedicine in our practice. It helps with accessibility—if patients can't get to the clinic or manage meds. It is used for routine follow-up."

—Rural internist

"I think the use of telehealth is very practice and insurance dependent. If they cut reimbursement, which they're starting to do, then I think it's not going to last very long. It's unfortunate because it is a very helpful tool."

—Gastroenterologist

Note: The market research and statistical analysis in this report were conducted in a manner consistent with industry standards and market research codes of conduct; however, this is in no way comparable to the scientific rigor of clinical research. All statistical significance in this report is at 95% confidence.

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"In gastroenterology, I think telehealth is great for triaging, that is, determining whether a patient should go to the emergency room or can stay home. There might be a larger role for it in other types of specialties."

—Gastroenterologist

"I did telehealth for a full year during COVID and really love it, so I still do it one day a week after advocating with my organization. I get so much work done."

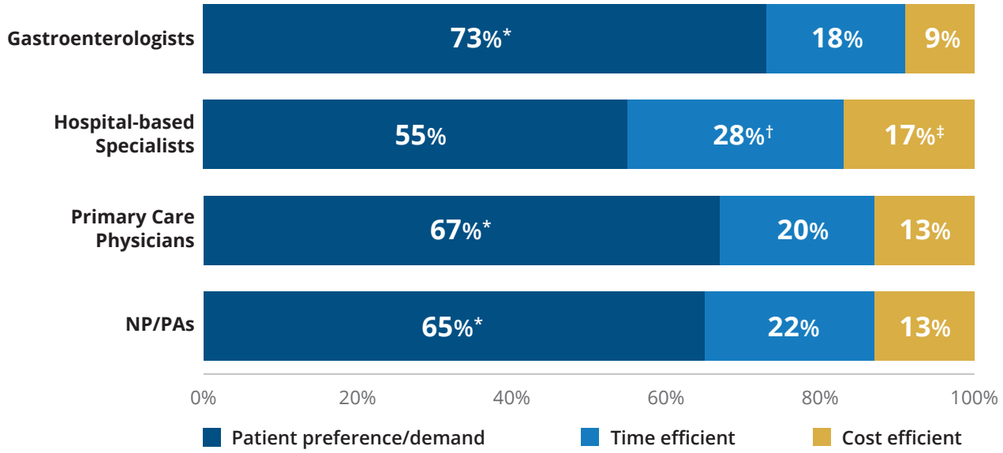
—Primary care physician

In Figure 41, respondents were asked to report on the reasons for the utilization of telemedicine for routine patient visits.

Patient demand and preference are driving telemedicine use. In the telephone interviews, providers shared that they will continue to offer telemedicine as long as it is reimbursed.

Figure 41 | **Drivers of Telemedicine Utilization for Routine Patient Visits**

Q3.29. Why are you using telemedicine for routine patient visits?



N=400 (100 Gastroenterologists, 100 Hospital-based Specialists, 100 PCPs, 100 NPs/PAs).
*This number is statistically significant at 95% confidence versus Hospital-based Specialists.
†This number is statistically significant at 95% confidence versus PCPs and Gastroenterologists.
‡This number is statistically significant at 95% confidence versus Gastroenterologists.

"The cons of telehealth is the pay—pay is less. And most things you can't treat as well via telehealth. Of course, now that [COVID's] all over, people are kind of demanding it because it is easier."

—Nurse practitioner

"We find that patients are more consistent with follow-up appointments if telehealth is available."

—Primary care physician

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Guidelines for the Management of Liver Disease

The following resources provide guidance to help improve quality and delivery of high-value care to those living with chronic liver disease and its complications.

AGA Clinical Care Pathway for the Risk Stratification and Management of Patients With Nonalcoholic Fatty Liver Disease by F Kanwal, JH Shubrook, LA Adams, et al. *Gastroenterology*. 2021;161(5):1657-1669.
AGA convened internal experts in nonalcoholic fatty liver disease to outline the spectrum of care from screening and diagnosis to patient care management.

American Association of Clinical Endocrinology Clinical Practice Guideline for the Diagnosis and Management of Nonalcoholic Fatty Liver Disease in Primary Care and Endocrinology Clinical Settings: Co-sponsored by the American Association for the Study of Liver Diseases (AASLD) by K Cusi, S Isaacs, D Barb, et al. *Endocr Pract*. 2022;28(5):528-562.
Provides evidence-based recommendations regarding the diagnosis and management of nonalcoholic fatty liver disease and nonalcoholic steatohepatitis to endocrinologists, primary care clinicians, health care professionals, and other stakeholders.

Development of Quality Measures in Cirrhosis by the Practice Metrics Committee of the American Association for the Study of Liver Diseases by F Kanwal, EB Tapper, C Ho, et al. *Hepatology*. 2019;69(4):1787-1797.
This is an explicit set of evidence-based quality measures for adult patients with cirrhosis. These measures are a tool for providers and institutions to evaluate their care quality, drive quality improvement, and deliver high-value cirrhosis care. The quality measures are intended to be applicable in any clinical care setting in which care for patients with cirrhosis is provided.

The Diagnosis and Management of Nonalcoholic Fatty Liver Disease: Practice Guidance From the American Association for the Study of Liver Diseases by N Chalasani, Z Younossi, JE Lavine, et al. *Hepatology*. 2018;67(1):328-357.
This guidance provides a data-supported approach to the diagnostic, therapeutic, and preventive aspects of nonalcoholic fatty liver disease care and was created to help clinicians understand and implement the most recent evidence. (This replaces the 2012 edition.)

Diagnosis, Evaluation, and Management of Ascites, Spontaneous Bacterial Peritonitis and Hepatorenal Syndrome: 2021 Practice Guidance by the American Association for the Study of Liver Diseases by SW Biggins, P Angeli, G Garcia-Tsao, et al. *Hepatology*. 2021;74(2):1014-1048.
This is a comprehensive guidance on the diagnosis, evaluation, and management of ascites and hepatorenal syndrome (HRS) in patients with chronic liver disease. (This replaces the 2012 edition.)

Hepatic Encephalopathy in Chronic Liver Disease: 2014 Practice Guideline by the American Association for the Study of Liver Diseases and the European Association for the Study of the Liver by H Vilstrup, P Amodio, J Bajaj, et al. *Hepatology*. 2014;60(2):715-735.
Intended for use by physicians, these recommendations suggest preferred approaches to the diagnostic, therapeutic, and preventive aspects of care for patients with hepatic encephalopathy.

A Multi-society Delhi Consensus Statement on New Fatty Liver Disease Nomenclature by ME Rinella, JV Lazarus, V Ratziu, et al. *Hepatology*. June 24, 2023. doi:10.1097/HEP.0000000000000520

Portal Hypertensive Bleeding in Cirrhosis: Risk Stratification, Diagnosis, and Management: 2016 Practice Guidance by the American Association for the Study of Liver Diseases by G Garcia-Tsao, JG Abraldes, A Berzigotti, and J Bosch. *Hepatology*. 2017;65(1):310-335.
Provides a data-supported approach to risk stratification, diagnosis, and management of patients with cirrhosis and portal hypertension.

US NASH Action Plan from the Global Liver Institute and the NASH Council. Published December 2020. https://static1.squarespace.com/static/53bafd3ce4b0ae714af7153f/t/5fdcc2f037b4b658917832f3/1608303368832/us-nash-action-plan-global-liver-institute-nash-council.pdf
A roadmap for addressing NASH with recommendations for meaningful activities for relevant stakeholder groups: patients/care partners, clinicians, medical societies, patient advocacy organizations, industry, payers, health systems, regulators, and policymakers.

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Foundations and Websites

American Association for the Study of Liver Diseases (AASLD)
aasld.org
The leading organization committed to preventing and curing liver disease. The website contains journals, practice guidelines, programs initiatives, and more to promote liver health and quality patient care.

American Liver Foundation
liverfoundation.org
Provides education and support services to the 30 million Americans affected by liver disease and helps to fund critical research with the goal of making liver disease a thing of the past.

Chronic Liver Disease Foundation (CLDF)
chronicliverdisease.org
Provides health care professionals and patients with the most current information on chronic liver disease through educational and outreach programs. These programs are designed so physicians, advanced practice providers, nurses, pharmacists, and all other similar health care providers have information about the latest medical developments and their implications for patient care.

Global Liver Institute
globalliver.org
The mission of the Global Liver Institute is to improve the lives of individuals and families impacted by liver disease through promoting innovation, encouraging collaboration, and scaling optimal approaches to help eradicate liver diseases.

Salix-sponsored Websites

ACE for Health Systems
AccessClickEngage.liverhealthnow.com/HS
Get access to EHR platforms filled with health resources to help identify, manage, and transition patients with overt hepatic encephalopathy while they are in the hospital.

ACE for Long-term Care
AccessClickEngage.liverhealthnow.com/LTC
Get access to EHR platforms filled with health resources to help you identify and manage patients with cirrhosis and overt hepatic encephalopathy in long-term care.

LiverHealthNow/Ambulatory Care
LiverHealthNow.com/AC
This website provides a variety of evidence-based provider and patient resources that can help identify, manage, and effectively transition patients with chronic liver disease.

LiverHealthNow/Primary Care
LiverHealthNow.com/PC
This website provides health resources that help PCPs identify and manage patients with chronic liver disease in a primary care practice.

UnderstandingHE
UnderstandingHE.com
This patient/caregiver website helps inform both audiences about exactly what hepatic encephalopathy is and what steps can be taken to manage it.

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Appendix

Figures and Tables Index

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Salix Pharmaceuticals

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