

**Title:** Exploring changing attitudes to non-invasive liver fibrosis tests in secondary care pathways: comparison of two national surveys.

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KWMA: conceptualization, methodology, validation, formal analysis, data curation, writing – original draft, review & editing; AS: conceptualization, methodology, validation, writing – review & editing; IAR: writing – review & editing; HJ: writing – review & editing; SR: writing – review & editing; AY: writing –review & editing; JFD: writing –review & editing; WR: conceptualization, methodology, writing – review & editing, supervision.

**Keywords:** non-invasive liver tests, fibrosis assessment, FIB-4, enhanced liver fibrosis test, transient elastography

## **Abstract**

**Introduction:** The increasing availability of non-invasive liver tests (NITs) has created the opportunity to explore their use in improving risk stratification of advanced liver disease. The study aimed to determine the attitudes and practices amongst UK secondary care specialists, focusing primarily on attitudes to fibrosis assessment and the use of NITs.

**Methods:** Two web-based surveys were circulated, first between 2014-2015 (Survey 1), and again in 2021 (Survey 2). The surveys were promoted via the British Society of Gastroenterology, the British Association for the Study of the Liver, and using Twitter®.

**Results:** In Survey 1, 215 healthcare professionals (HCPs) completed the online survey. 112 HCPs completed Survey 2. 71 acute UK trusts were represented in Survey 1 compared to 60 trusts in Survey 2. Between the two surveys, the proportion of HCPs performing fibrosis assessment in all or nearly all cases rose from 45.1% to 74.1% ( $\chi^2=25.01$ ;  $p<0.0001$ ). 46.5% ( $n=33/71$ ) respondents in acute services reported the use of NITs in clinical pathways in Survey 1, rising to 70.0% ( $n=42/60$ ) in Survey 2 ( $\chi^2=7.35$ ;  $p=0.007$ ). Availability of tests has increased but is not universal. The proportion reporting availability as a barrier to uptake fell from 57.2% of responses in Survey 1 to 38.4% in 2021 ( $\chi^2=11.01$ ;  $p=0.0009$ ).

**Conclusion:** Between 2014 and 2021, the role of NITs in fibrosis assessment has risen substantially, as has the proportion of clinicians using NITs in clinical pathways to assess risk of liver disease. Poor access to NITs remains the predominant barrier.

## **Introduction**

A combination of rising morbidity and mortality associated with chronic liver disease coupled with an ever-increasing burden on healthcare systems demands innovative strategies to improve patient outcomes (1, 2). This has only been compounded by the legacy of the COVID19 pandemic, with increasing rates of alcohol use and obesity within the population, twinned with rising waiting list times (3-5).

Patients are frequently diagnosed with liver disease at the later stages of the condition which limits treatment options and may have a negative impact on patient prognosis (6-8). This can be due to inherent barriers to detecting liver disease. In the “standard of care” model, opportunistic testing in primary care lacks sufficient sensitivity and specificity to detect advanced fibrosis and cirrhosis, contributing to delayed recognition of advanced liver disease. The expanding body of evidence suggests that morbidity and mortality increases substantially with the development of advanced fibrosis and liver cirrhosis (9-11). The evolution and increasing availability of non-invasive liver tests (NITs) including non-invasive liver fibrosis blood tests e.g. Fibrosis-4 (FIB-4), NAFLD Fibrosis Score (NFS) and Enhanced Liver Fibrosis (ELF®) test, and transient elastography (TE) techniques e.g. FibroScan® has created the opportunity to explore the use of NIT to improve early detection of advanced liver disease in community settings.

To understand better the practical utilities of early detection strategies, we surveyed gastroenterology and hepatology healthcare workers across the UK, first in 2014-2015 and then in 2021. The aim of these national surveys was to determine the attitudes and practices of secondary care specialists involved in the management of patients with liver disease in the UK, focusing primarily on their attitudes to liver fibrosis assessment and the use of NITs. Secondary aims included exploring their knowledge and use of NITs, and their use in designated liver disease detection and risk stratification pathways. Finally, the study sought to understand how these attitudes have changed with increasing knowledge in this area and post onset of the COVID19 pandemic.

## Methods

*Survey design.* This study of practice and perception of liver fibrosis assessment and the role of non-invasive liver fibrosis tests was interrogated through a cross-sectional survey. The survey was designed to explore the following themes:

- (1) Respondent demographics (healthcare role, grade, location).
- (2) Current practice of liver fibrosis assessment (including role of liver biopsy and NITs).
- (3) The potential of NITs to determine liver fibrosis severity in clinical practice.
- (4) The barriers to implementation of NITs in clinical practice.
- (5) The use of NITs in clinical pathways.

The answers were either orientated (choice of different options), matrix of choices (multiple answers per row), semi-quantitative (“never”, “up to a quarter” etc.), or open-ended (unrestricted free text).

*Survey dissemination.* Two, almost identical, web-based surveys were circulated (see supplementary material S.1 and S.2). The original survey (Survey 1) was circulated between 1<sup>st</sup> October 2014 to 1<sup>st</sup> October 2015. The second survey (Survey 2) was circulated between 1<sup>st</sup> November and 24<sup>th</sup> December 2021. A pragmatic decision was made to close the second survey early as the UK National Health Service (NHS) was experiencing a surge in patient caseload related to the *Omicron* variant of COVID-19. Gastroenterology and hepatology specialists involved in the care of patients with chronic liver disease were approached via different routes, including promotion of the surveys via the British Society of Gastroenterology, the British Association for the Study of the Liver, and using the Twitter® social media platform. Respondent confidentiality was maintained as responses to the survey were anonymous (unless the respondent chose to declare personal details in the comments section).

*Statistical analysis.* Standard descriptive statistics were used to analyse the data, including counts and percentages for categorical data and median and range for non-normally distributed data. Chi<sup>2</sup> test was used to examine the difference in proportions of categorical variables between the survey results at the 2014 and 2021 time point, with a significance level of 5%.

A sensitivity analysis was conducted of respondents who completed both Survey 1 and 2 to explore if overall findings could be replicated to more convincingly determine if changes in attitudes and practice had occurred.

## Results

During the first circulation of the survey between 1<sup>st</sup> October 2014 to 1<sup>st</sup> October 2015, 215 healthcare professionals completed the online survey (see Table 1.). Hepatologists constituted 106 (49.5%) respondents, 96 (44.9%) were gastroenterologists and 12 (5.6%) were 'others' including internal medicine specialists. 112 health care professionals completed the repeat survey between 1<sup>st</sup> November and 24<sup>th</sup> December 2021. In this survey hepatologists constituted 72 (64.3%) respondents, 36 (32.1%) were gastroenterologists and 5 (4.5%) were 'others' including internal medicine specialists. In 2014-2015 approximately two-thirds of respondents were consultants (139 respondents; 64.7%) compared to almost three quarters of respondents in 2021 (82 respondents; 72.6%).

In Survey 1, responses covered 63 of 152 (41.4%) acute English NHS healthcare trusts. An additional 8 Trusts were represented from the rest of the United Kingdom (4 from Scotland, 3 from Wales, 1 from Northern Ireland). In Survey 2, responses were received from healthcare professionals covering 34.9% (n=53) acute English NHS healthcare trusts, with a further 7 Trusts from the other home nations (5 from Scotland, 1 from Wales and 1 from Northern Ireland).

### *The role of liver fibrosis assessment in patients with liver disease*

In Survey 1, 206/215 respondents (95.8%) performed liver fibrosis assessment in a proportion of their liver patients. In Survey 2, 110/112 (98.2%) performed fibrosis assessment in their patients (see Figure 1.). The proportion of individuals that performed fibrosis assessment in all or nearly all cases rose significantly by almost two-thirds between 2014 and 2021 from 45.1% (n=97/215) to 74.1% (n=83/112;  $\chi^2=25.01$ ;  $p<0.0001$ ). Conversely the number of clinicians assessing fibrosis in  $\leq 25\%$  of their patients fell more than 3-fold from 26.5% (n=57/215) to 8.0% (n=9/112) between the two surveys .

### *The use of non-invasive tests in clinical pathways*

In 2014-2015, respondents representing 33/71 (46.5%) UK healthcare Trusts or CCGs reported the use of non-invasive fibrosis tests in clinical pathways. In 2021, respondents from 60 UK acute trusts answered whether a clinical pathway was established, of which 42 (70.0%;  $\chi^2=7.35$ ;  $p=0.007$ ) reported using a primary or secondary care pathway. In 2021, pathways described in free text included:

*“NAFLD risk stratification pathway based on Camden & Islington pathway.”*

*“Direct access to fibroscan referral from primary care if evidence of alcohol dependency.”*

#### *The role of liver biopsy in patients with liver disease*

Respondents reported that liver biopsy remains an important investigative tool in the management of patients with liver disease (see Figure 2.). In Survey 1, 30.6% (n=66/215) of respondents used liver biopsy solely for liver fibrosis assessment, which was almost 3 times higher than in Survey 2 (11.6%; n=13/112;  $\chi^2=14.65$ ; p=0.0001). Diagnosing aetiology of liver disease remained the commonest reason for biopsy between the two surveys: 85.1% (n=183/215) in 2014-2015 and 84.8% (n=95/112;  $\chi^2=0.00$ ; p=0.943) in 2021. The second commonest reason in Survey 1 and 2 was guiding treatment decisions, 85.1% (n=183/215) and 75% (n=85/112;  $\chi^2=4.24$ ; p=0.040) respectively.

Thematic analysis of free text highlighted the important but diminishing role of biopsy in the context of fibrosis assessment, with one respondent in Survey 1 commenting, *“Liver biopsy now second or third line for fibrosis staging and more important in acute liver dysfunction rather than in chronic disease”*. Whilst in Survey 2, a hepatologist respondent stated liver biopsy *“rarely happens”* for fibrosis assessment alone.

#### *The potential for non-invasive liver fibrosis tests as a suitable alternative to liver biopsy*

In Survey 1, the majority of respondents (82.8%; n=178/215) agreed non-invasive liver fibrosis tests to be a suitable alternative to liver biopsy for fibrosis assessment, whilst 29/215 (13.4%) saw them as a useful adjunct (see Table 2.). Only 5 respondents (2.3%) felt non-invasive assessment had no role in clinical practice. By 2021, 93.7% (n=105/112) of respondents agreed non-invasive fibrosis tests were a suitable alternative to biopsy for fibrosis assessment, and the remaining 6.3% (n=7/112) of respondents felt it was a useful adjunct.

The perception of NITs as a suitable alternative for liver biopsy to allow assessment of prognosis in patients with liver disease increased from 66.0% (n=138/215) to 79.5% (n=89/112;  $\chi^2=8.10$ ; p=0.004). With regards to guiding treatment decisions, 116

respondents (55.0%) felt NITs were a suitable alternative to liver biopsy in Survey 1, whilst 57 (27.8%) saw them as a useful adjunct and 14 (6.7%) felt they had little role in guiding treatment. This pattern of opinion remained largely similar in Survey 2, with 56.2% (n=63/112), 32.1% (n=36/112) and 10.7% (n=12/112) of respondents stating NITs were a suitable alternative to 48 liver biopsy, useful adjunct and had no role in guiding treatment, respectively. A comparable spread of views were observed when gauging if NITs were considered a suitable alternative to liver biopsy to assess response to treatment; in Survey 1 48.4% (n=104/215) felt it was a suitable adjunct with only 28.8% (n=62/215) stating NITs were not useful compared to 42.9% (n=48/215) and 22.3% (n=25/112) respectively in Survey 2. In the scenario of discordance between non-invasive fibrosis tests results and the clinical picture, liver biopsy was considered to be the preferred “gold standard”.

#### *Clinical methods to diagnose liver fibrosis in current clinical practice*

Respondents were asked to consider the methods they employ to assess a patient's liver fibrosis stage. Responses to different fibrosis assessments are detailed in Table 3. The proportion of respondents who considered FIB-4 to be useful in fibrosis assessment doubled from 40.7% (n=87/215) in 2014 to 83.0% (n=93/112;  $\chi^2 = 53.93$ ;  $p < 0.0001$ ) in 2021. ELF was also more favourably viewed amongst respondents for fibrosis assessment, increasing from 25.3% (n=54/215) using it in 2014 to 43.7% (n=49/112;  $\chi^2 = 11.85$ ;  $p = 0.0006$ ) using it 2021. Notably a further 49.1% (n=55/112) of respondents considered ELF useful but did not use it in their practice in 2021. In 2014 87.0% (n=187/215) considered TE useful for fibrosis assessment, rising to almost all respondents (95.5%; n=107/112;  $\chi^2 = 5.96$ ,  $p = 0.148$ ).

#### *Liver fibrosis assessment by aetiology*

The survey evaluated the influence of aetiology of liver disease on the need for fibrosis assessment. Irrespective of the aetiology, fibrosis assessment was considered an integral part of disease management in the majority of cases. Fibrosis assessment with imaging e.g. elastography techniques including TE were the preferred methods of choice in HCV (64.5% in 2014-2015 vs 88.4% in 2021 respectively;  $\chi^2 = 20.95$ ;  $p < 0.0001$ ), HBV (51.2% vs 89.3%;  $\chi^2 = 46.58$ ;  $p < 0.0001$ ), ARLD (49.8% vs 80.4%;  $\chi^2 = 28.77$ ;  $p < 0.0001$ ). In NAFLD the majority of fibrosis assessments were also through elastography techniques (51.9% in 2014-2015 vs 71.4% in 2021;  $\chi^2 = 11.88$ ;

p=0.0006), with a similar proportion of fibrosis assessments were using serum fibrosis scores (20.9% in 2014-2015 vs 23.2% in 2021;  $\chi^2=0.23$ ; p=0.635). Between 2014-2015 and 2021 the attitudes towards liver biopsy for fibrosis assessment in viral hepatitis, ARLD and NAFLD had changed with far less biopsies being performed in 2021. Liver biopsy continues to dominate fibrosis assessment in autoimmune liver diseases, e.g. 69.3% of respondents biopsied their patients with autoimmune hepatitis in 2014 compared to 54.5% in 2021.

#### *Barriers to the implementation of non-invasive liver fibrosis tests in clinical practice.*

The survey explored current access to non-invasive fibrosis tests in the UK. In Survey 1, only 52/215 participants (24.2%) reported adequate access to non-invasive fibrosis tests, with the majority declaring suboptimal access. This proportion had doubled by 2021 to 50% (n=56/112;  $\chi^2=22.18$ ; p<0.0001). By Survey 2, the major barrier to using NITs in clinical practice was the availability of the test, with 38.4% of respondents citing this as the main reason for not employing these tests (n=43/112).

The barriers to using non-invasive fibrosis tests are summarised in Figure 3. Lack of local availability of fibrosis tests was the commonest reason in both surveys (58.9% in 2014 vs 38.4% in 2021;  $\chi^2=11.01$ ; p=0.0009). In Survey 1, a substantial proportion (17.8%) had concerns regarding the existing non-invasive fibrosis tests with regards to reliability in diagnostic accuracy and clinical utility, but this proportion had halved to 9.8% by Survey 2 ( $\chi^2=3.56$ ; p=0.059). Cost of tests was a common barrier, cited by 30.2% of clinicians in Survey 1, but this had also fallen to 8.9% ( $\chi^2=18.91$ ; p=0.0001) by Survey 2. In 2021, 50% of respondents stated they had suitable access to non-invasive fibrosis assessment, compared to 24.2% in 2014-2015 ( $\chi^2 = 22.18$ , p<0.0001). Sample participant comments included:

*“Only 1 centre in Scotland has access to ELF. Availability limited by cost, I believe.”*

*“High DNA (did not attend appointment) rate for follow up after a hospital presentation. Direct GP referrals have a higher attendance though.”*

*“Poor local dissemination of Primary Care referral pathways (ELF test is routinely available locally in primary care). Limited Fibroscan capacity in Secondary Care”*

#### *Impact of COVID19 on service delivery*



Respondents were asked, in the event of using transient elastography for fibrosis assessment, had they had to reduce capacity to accommodate social distancing measures. Of those that used TE, 38.8% (n=50/103) stated they had to reduce capacity with 3 respondents saying this had to be less than 50% service capacity. 10 respondents changed their fibrosis assessment strategy to not include TE. 51.5% of respondents (n=53/103) using TE stated they remained at full capacity despite social distancing measures.

#### *Sensitivity analysis*

Respondents from 36 acute trusts in the UK, representing 3 home nations responded to Survey 1 (n=85) and Survey 2 (n=46). In this subgroup, the proportion of individuals that performed fibrosis assessment in all or nearly all cases rose from 8.2% in Survey 1 (n=7/85) to 26.1% (n=12/46;  $\chi^2 = 7.67$ , p=0.006). The proportion of respondents who had adopted pathways increased substantially from 52.9% (n=45/85) to 76% (n=35/46;  $\chi^2 = 6.72$ , p=0.01).

A similar reporting pattern of barriers to implementing the use of NITs was seen between Survey 1 and Survey 2. These included a reduction in concerns regarding cost (34.1% in Survey 1 vs 13% in Survey 2;  $\chi^2 = 6.77$ , p=0.009) and concerns regarding diagnostic accuracy of NITs (29.4% in Survey 1 vs 6.5% in Survey 2;  $\chi^2 = 9.31$ , p=0.002). There was a trend towards reduced concerns surrounding a lack of availability of NITs (57.6% in Survey 1 vs 43.5% in Survey 2;  $\chi^2 = 2.40$ , p=0.12).

## Discussion

### *Main findings*

The two surveys performed six years apart and pre- and post-COVID19 pandemic demonstrate that fibrosis assessment in the evaluation of patients at risk of chronic liver disease has become more routine amongst clinicians managing liver disease in 2021. The majority of clinicians now state NITs are a useful alternative to liver biopsy for fibrosis assessment in 2021 coupled with a trend for liver biopsy to be used more sparingly in 2021 compared to 2014-2015. The use of blood test fibrosis markers such as FIB-4 and ELF for fibrosis assessment had increased significantly amongst clinicians between the two surveys. Transient elastography usage for fibrosis assessment remained high, with a prominent role in assessing patients with viral hepatitis, ARLD and NAFLD in 2021 compared to 2014-2015. This coincides with an increasing consensus regarding the role of TE and rising liver stiffness measurement in excluding or ruling in advanced fibrosis, compensated advanced chronic liver disease and clinically significant portal hypertension (12-14). Furthermore, there is a growing consensus that a two-step risk stratification with NITs in the general population provides high diagnostic accuracy for detecting fibrosis (15, 16). The rise in use of non-invasive markers such as FIB-4 between the two surveys perhaps reflects the high negative predictive value (>90%) a result of <1.3 provides for excluding fibrosis (17). These have now been incorporated into national and international guidelines for the management of abnormal liver blood tests and liver disease evaluation (18, 19).

There was an increase in the proportion of clinicians who considered NITs a suitable alternative to liver biopsy when assessing liver disease prognosis. The view of the role of liver biopsy has shifted within the six-year interval reflecting current international guidance on the use of NITs for fibrosis assessment and risk stratification (14). Liver biopsy continued to be preferred in situations of discordance between NITs and the clinical picture, as well as autoimmune liver disease assessment.

The attitudes to liver biopsy versus NITs when considering guiding treatment decisions remained broadly similar over the six-year time point with over half of respondents stating NITs were a suitable alternative to liver biopsy. The proportion of respondents who felt NITs were a suitable alternative to liver biopsy when guiding treatment response trended down between the two surveys. Unsurprisingly, liver biopsy remains central for diagnosis of liver disease aetiology between the two surveys, reflecting its role as the gold standard diagnostic tool (20). This survey did

not explore the important role liver biopsy plays in acute liver failure, such as excluding aetiologies that would preclude transplantation.

There was a significant increase in the proportion of clinicians reporting that community pathways were in place, utilising non-invasive tests, between the two time points. This reflects a growing trend internationally of embedding community based detection and risk stratification pathways to identify advanced fibrosis and cirrhosis early. Such clinical pathways have repeatedly been demonstrated to be cost effective, reduce unnecessary referrals and detect liver disease early, facilitating life style interventions (21-25). Whether early detection of liver disease changes liver-related outcomes requires long term prospective data and on-going research.

### *Strengths and Limitations*

To the best of our knowledge this is one of the first surveys of clinicians about attitudes related to fibrosis assessments in liver disease comparing survey results between two distinct time points pre and post pandemic.

There are limitations to the study. The 2021 survey only ran for 6 weeks compared to the 2014-2015 survey which ran for 1 year. This marked difference was related to the timing of the 2021 survey circulation, shortly after followed by a surge of coronavirus Omicron variant related hospital admissions in the UK. This impaired the ability to promote the survey whilst our audience of interest, secondary care clinicians, were experiencing a particularly high clinical workload. As a result less than 40% of acute hospital trusts were represented in the survey in 2021. Both surveys did not provide good representation of clinician responses from the devolved nations meaning our results largely reflect the experience of clinicians in England.

The number of responses in 2021 was just over half the responses in 2014, therefore proportions of change in response to the questionnaire reported between the two time points have to be interpreted in that context.

It is also plausible that clinicians interested in this topic would be more likely to respond to the surveys. To address this, a sensitivity analysis of respondents to both surveys did replicate similar trends in fibrosis assessment, adoption of community pathways and attitudes towards barriers in NIT implementation.

### *Other evidence*

When examining pathways in primary or secondary care that utilise NITs of liver fibrosis to guide management of patients with, or at risk of liver disease, we found 65.2% of respondents, representing 40.1% of acute hospital trusts, stating they did have a pathway in place in 2021. This contradicts a recent comprehensive cross-sectional study by Jarvis *et al* of 99% clinical commissioning groups (CCGs) and health boards in the UK in 2020 (26). The authors found 40% had a primary care pathway to evaluate abnormal liver blood tests and 29% had a pathway to manage common liver diseases (26). The survey by Jarvis *et al* achieved greater national coverage than our study, but the disparity is interesting, and may be attributable to the differences in the groups targeted by the two studies. While the present survey targeted specialists in secondary care accepting referrals from primary care, Jarvis *et al.* targeted CCGs. The disparity in the findings of the two studies suggests that secondary care physicians may have developed pathways but are not implementing them in collaboration with primary care practitioners effectively. This then creates a perception amongst primary care providers that there is no mechanism in place to detect and manage patients at risk of common liver diseases. This is crucial as primary care practitioners will be reviewing the vast majority of patients with abnormal liver blood tests and suspected NAFLD or ARLD in the first instance (27, 28). Qualitative research from Standing *et al* illustrated that liver disease was not a priority for primary care physicians, and interpretation of abnormal liver blood tests was often a source of concern (29). This would be ameliorated by better coordination between primary and a secondary care teams to implement detection and risk stratification strategies including dedicated education programmes and establishing local liver champions (30).

Whilst the proportion of respondents reporting better access to NITs between the two surveys, the proportion remained low at 50%. This is corroborated by Jarvis *et al* in their survey of CCGs and health boards in the UK, with substantial regional variation. For example, direct serum fibrosis markers such as enhanced liver fibrosis (ELF) test, were utilised by 13% of CCGs in England versus 50% of Scottish health boards (26). This is despite ELF test being recommended by the National Institute of Clinical Excellence (NICE) guidelines for risk stratification in patients with NAFLD (31). Attempts to rectify these inequalities in access has been facilitated through the National Pathology Exchange hosted by the NHS, allowing any lab across the UK to request and access an ELF test (32). Similar accessibility issues were found with TE, with only 19% of CCGs in England having access compared to all health boards in

Wales (100%) (26). NICE is set to publish guidance supporting the use of TE in the primary and community care setting in 2023 which should also begin to ameliorate issues around accessibility (33). Related to this, the British Liver Trust campaign to “*Make early diagnosis of liver disease routine*” is seeking to rectify inequity across the UK to accessing liver services, encouraging Integrated Care Systems (formerly CCGs) to adopt early detection pathways (34).

Whilst over 50% of respondents continued the TE clinics at full capacity during the COVID19 pandemic, almost 40% of respondents in 2021 reported having to reduce TE capacity in the context of maintaining social distancing measures. How changes like this impacts gastroenterology and hepatology services is unknown. This is occurring at a period where clinicians are facing significant pressure to address NHS waiting times (5), lower health utilisation during the pandemic risks patients presenting later with symptoms (35), and rising levels of alcohol use and obesity to compound the current situation.

## **Conclusion**

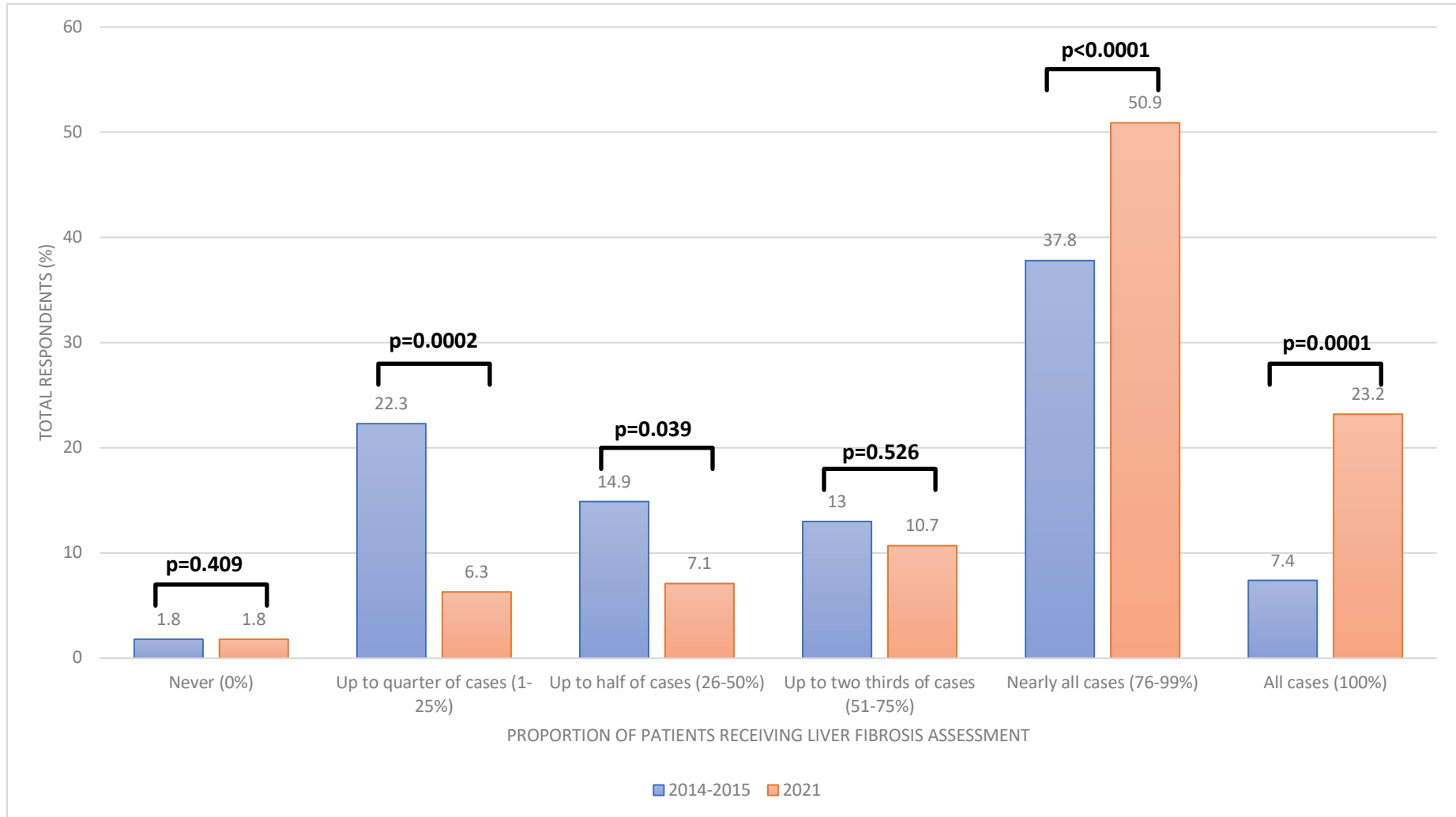
Between 2014 and 2021, the role of NITs in fibrosis assessment has risen substantially, as has the proportion of clinicians using NITs in clinical pathways to guide the management of liver disease and those at risk of it. Poor access to NITs remains the predominant barrier. A simple, coordinated national strategy in collaboration with primary care is vital to ensure individuals at risk of cirrhosis can be identified easily and receive specialist input and interventions promptly.

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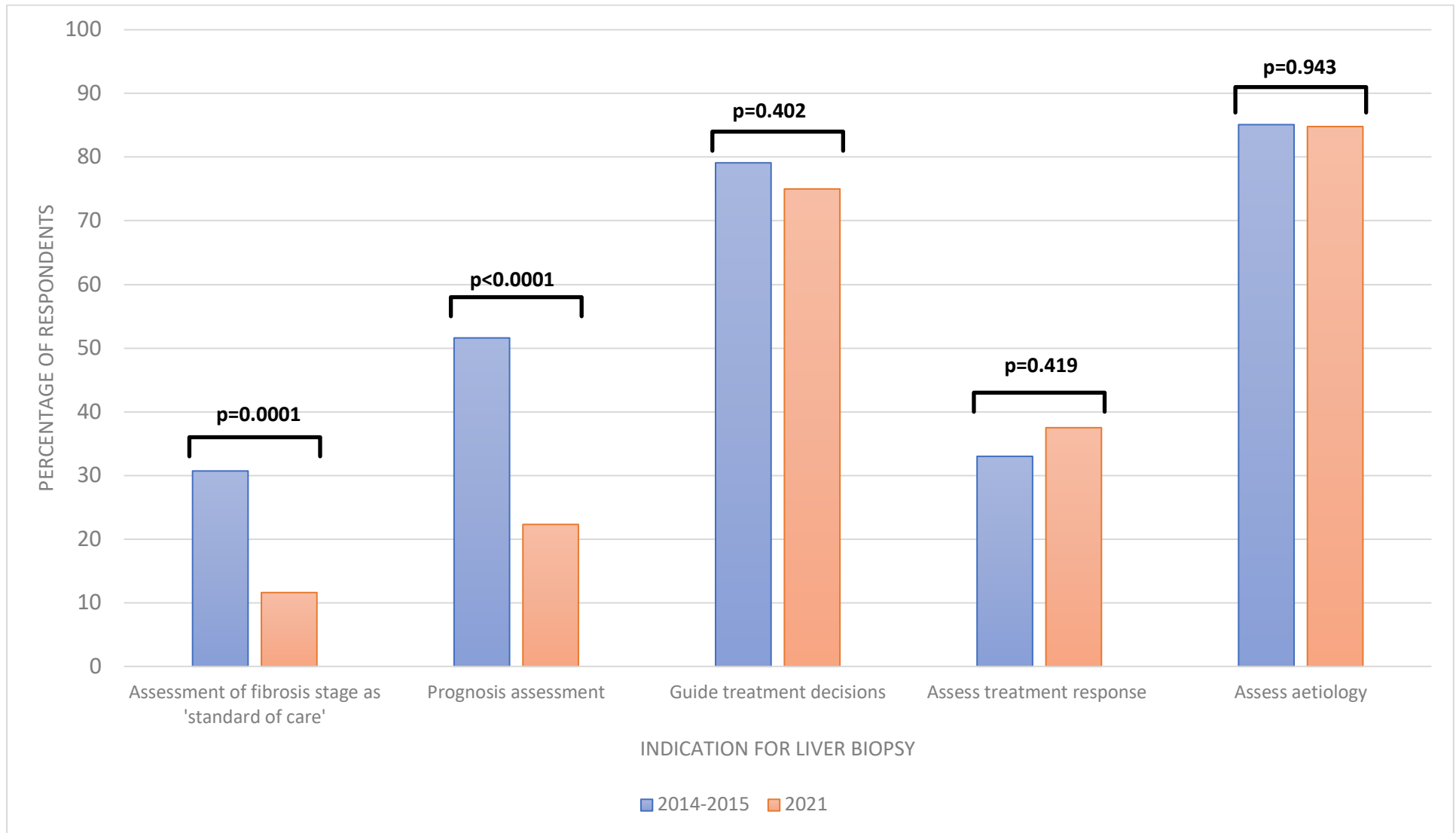
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**Figure 1.** Proportion of patients in whom physicians perform liver fibrosis assessment

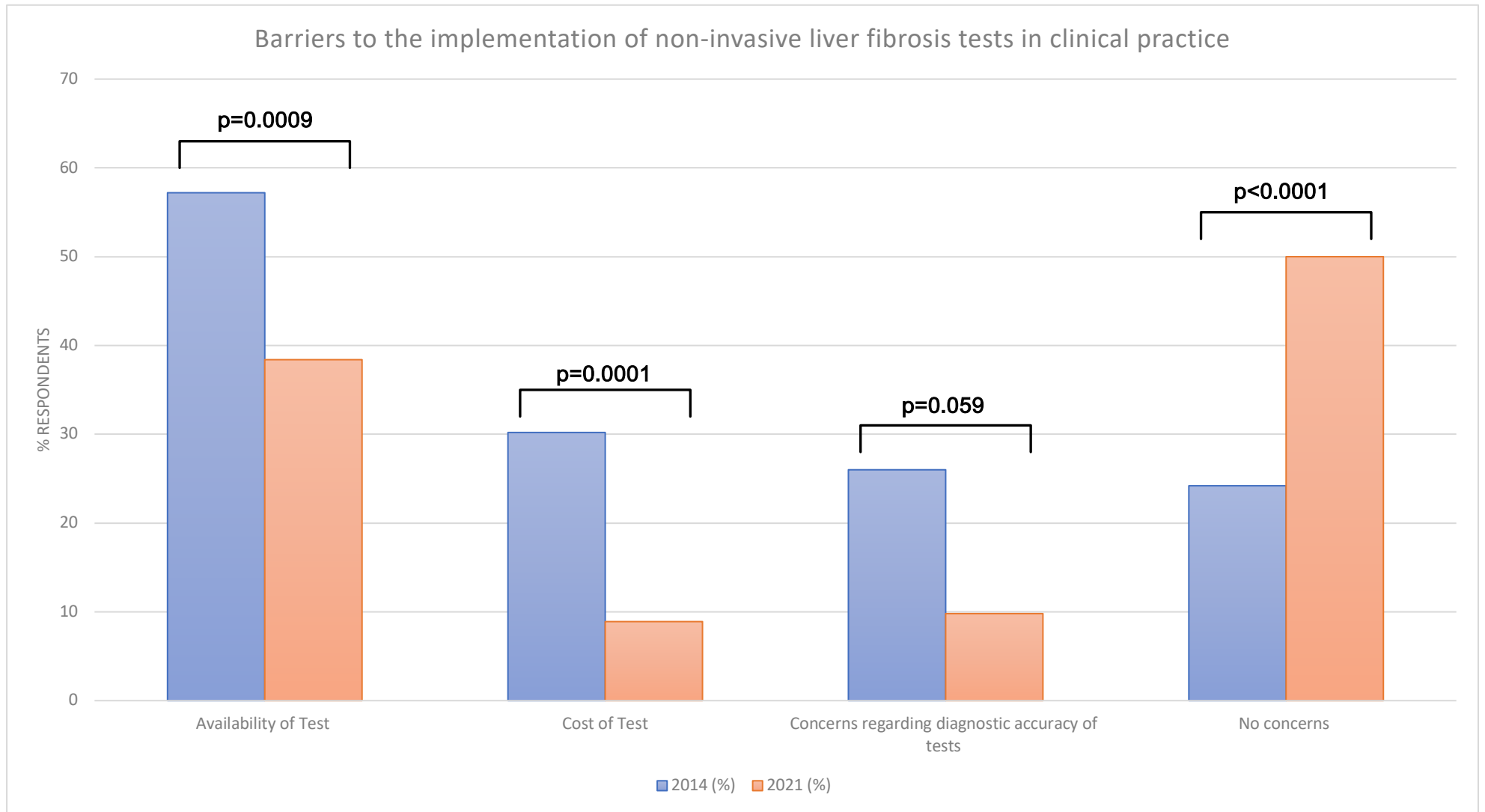




**Figure 2.** Indications for requesting liver biopsy in clinical practice.



**Figure 3.** Barriers identified to the implementation of non-invasive liver fibrosis



**Table 1.** Respondents to survey in 2014-2015 & 2021.

		<b>2014-2015 (%)</b>	<b>2021(%)</b>
<b>Specialty</b>	Gastroenterology	95 (44.2)	35 (31.2)
	Hepatology	106 (49.3)	72 (64.3)
	Other	11 (5.1)	5 (4.5)
<b>Role</b>	Consultant	136 (63.3)	82 (73.3)
	Nurse Specialist	16 (7.4)	7 (6.2)
	Specialty Trainee	56 (26.0)	22 (19.6 )
	Other	6 (2.8)	1 (0.9)

**Table 2** The potential of non-invasive liver fibrosis tests as an alternative to liver biopsy.

	NITs a suitable alternative to liver biopsy		NITs useful only as an adjunct to biopsy		NITs not useful	
	2014-2015	2021	2014-2015	2021	2014-2015	2021
<b>Assessing aetiology (n)</b>	4.7% (10)	9% (10)	27% (58)	31.5% (35)	65.1% (140)	59.8% (66)
<b>Assessing treatment response (n)</b>	49.8% (107)	42.9% (48)	20.6% (44)	34.8% (39)	29.7% (64)	22.3% (25)
<b>Guiding treatment decisions (n)</b>	54% (116)	56.2% (63)	37.7% (81)	32.1% (36)	6.5% (14)	10.7% (12)
<b>Prognosis assessment (n)</b>	64.2% (138)	79.5% (89)	26.5% (57)	13.4% (15)	6.5% (14)	5.4% (6)
<b>Assessment of fibrosis stage (n)</b>	82.8% (178)	93.7% (105)	13.5% (29)	6.3% (7)	2.3% (5)	0% (-)

**Footnote:** 215 responses received from Survey 1 in 2014-2015; 112 responses received from Survey 2 in 2021. These were the denominators used for respective surveys. Not all participants responded to each modality stated in question.

**Abbreviations:** NITs – non-invasive tests.

**Table 3.** Evaluation of current diagnostic methods to assess liver fibrosis stage

	Unaware of test		Not useful for fibrosis assessment		Use in clinical practice for fibrosis assessment but do not use		Useful for liver fibrosis assessment	
	2014-2015	2021	2014-2015	2021	2014-2015	2021	2014-2015	2021
<b>Clinical Examination (n)</b>	0.9% (2)	0.9% (1)	49.8% (107)	40.2% (45)	47% (101)	2.7% (3)	1.9% (4)	56.2% (63)
<b>LFTs (n)</b>	0.9% (2)	0% (-)	65.6% (141)	66.1% (74)	29.8% (64)	4.5% (5)	3.3% (7)	28.6% (32)
<b>Synthetic function (n)</b>	0.9% (2)	0.9% (1)	37.2% (80)	25.9% (29)	59.5% (128)	3.6% (4)	1.9% (4)	68.7% (77)
<b>APRI (n)</b>	15.3% (32)	6.2% (7)	5.6% (12)	7.1% (8)	43.7% (94)	52.7% (59)	34.9% (75)	32.1% (36)
<b>FIB-4 (n)</b>	12.6% (27)	0% (-)	1.9% (4)	0.9% (1)	40.4% (87)	14.3% (16)	44.7% (96)	83.0% (93)
<b>NAFLD Fibrosis Score (n)</b>	5.6% (12)	2.8% (3)	1.9% (4)	0.9% (1)	58.1% (125)	33.9% (40)	34.0% (73)	60.7% (68)
<b>ELF (n)</b>	10.7% (23)	2.8% (3)	1.4% (3)	2.8% (3)	62.3% (134)	49.1% (55)	25.1% (54)	43.7% (49)
<b>VCTE (n)</b>	0% (-)	0% (-)	0% (-)	0% (-)	13.0% (28)	3.6% (4)	86.5% (184)	95.5% (107)
<b>ARFI (n)</b>		16.1% (18)		2.8% (3)		57.1% (64)		18.7% (21)
<b>Ultrasound (n)</b>	0% (-)	16.1% (18)	35.8% (77)	2.8% (3)	2.8% (6)	57.1% (64)	61.4% (132)	18.7% (21)
<b>CT (n)</b>	0.5% (1)	0% (-)	40% (86)	35.7% (40)	16.7% (36)	9.8% (11)	60.9% (140)	52.7% (59)
<b>MRI (n)</b>	0.9% (2)	0% (-)	29.8% (64)	33.9% (38)	25.1% (54)	17.0% (19)	42.3% (91)	48.2% (54)
<b>Liver biopsy (n)</b>	0% (-)	0% (-)	0 (-)	20.5% (23)	5.6% (12)	28.6% (32)	43.7% (94)	50.0% (56)

**Footnote:** 215 responses received from Survey 1 in 2014-2015; 112 responses received from Survey 2 in 2021. These were the denominators used for respective surveys. Not all participants responded to each modality stated in question.

**Abbreviations:** APRI - AST to Platelet Ratio Index; ARFI - Acoustic Radio Frequency Impulse; CT - computed tomography; ELF - Enhanced Liver Fibrosis test; FIB-4 – Fibrosis-4 score; LFTs – liver function tests; MRI – magnetic resonance imaging; VCTE – vibration controlled transient elastography.