NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

DIAGNOSTICS ASSESSMENT PROGRAMME

Diagnostics consultation document

MRI-based technologies for assessing non-alcoholic fatty liver disease

The National Institute for Health and Care Excellence (NICE) is producing guidance on using MRI-based technologies for assessing non-alcoholic fatty liver disease in the NHS in England. The diagnostics advisory committee has considered the evidence and the views of clinical and patient experts.

This document has been prepared for public consultation. It summarises the evidence and views that have been considered, and sets out the recommendations made by the committee. NICE invites comments from registered stakeholders, healthcare professionals and the public. This document should be read along with the evidence (the diagnostics assessment report, diagnostics assessment report addendum and erratum).

The advisory committee is interested in receiving comments on the following:

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?
- Are the recommendations sound, and a suitable basis for guidance to the NHS?

Equality issues

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the recommendations may need changing to meet these aims. In particular, please tell us if the recommendations:

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- could have a different effect on people protected by the equality legislation than on the wider population, for example by making it more difficult in practice for a specific group to access the technology
- could have any adverse effect on people with a particular disability or disabilities.

Please provide any relevant information or data you have about such effects and how they could be avoided or reduced.

Note that this document is not NICE's final guidance on MRI-based technologies for assessing non-alcoholic fatty liver disease. The recommendations in section 1 may change after consultation.

After consultation, the committee will meet again to consider the evidence, this document and comments from the consultation. After considering the comments, the committee will prepare its final recommendations, which will be the basis for NICE's guidance on the use of the technology in the NHS in England.

For further details, see the diagnostics assessment programme manual.

Key dates:

Closing date for comments: 14 July 2022

Second diagnostics advisory committee meeting: 28 July 2022

Issue date: June 2022

1 Recommendations

1.1 There is not enough evidence to recommend LiverMultiScan or magnetic resonance elastography (MRE) to assess non-alcoholic fatty liver disease (NAFLD) in people:

- with indeterminate or discordant results from previous fibrosis testing
- when transient elastography or acoustic radiation force impulse elastography (ARFI) is unsuitable or has not worked.

1.2 Further research is recommended (see the section on further research) to determine the accuracy of LiverMultiScan and MRE for assessing NAFLD and how test results affect decisions about care.

Why the committee made these recommendations

Assessing the extent of NAFLD can help to make decisions about care, for example, if lifestyle changes are needed or how often to monitor the condition. Sometimes a biopsy is needed, which is invasive and can have severe side effects like bleeding or death. LiverMultiScan and MRE are non-invasive MRI-based tests that aim to assess the extent of liver disease, help make decisions about care, and avoid biopsy use. LiverMultiScan aims to identify a stage of NAFLD called non-alcoholic steatohepatitis (NASH).

Clinical evidence on test accuracy is uncertain. There is no evidence on how MRE might affect care decisions for the people who would have it in the NHS. It is very unclear how diagnosing NASH with LiverMultiScan would affect care decisions. There are currently no medicines for treating NASH, but this may change in the future. There is only 1 study on the effect of using LiverMultiScan on the number of liver biopsies, which is of low quality.

MRE may be cost effective but the estimates are uncertain, largely because the cost of using MRE in the NHS is very uncertain. For LiverMultiScan, the cost-effectiveness estimates are higher than what NICE normally considers a cost-effective use of NHS resources.

More evidence is needed about test accuracy and how results affect decisions about care. Therefore, research is recommended.

2 The diagnostic tests

Clinical need and practice

The condition

2.1 Non-alcoholic fatty liver disease (NAFLD) is the term for a range of conditions caused by a build-up of fat in the liver. NAFLD develops in 4 stages:

- simple fatty liver (steatosis): a largely harmless build-up of fat in the liver cells
- non-alcoholic steatohepatitis (NASH): build-up of fat leads to inflammation
- fibrosis: persistent inflammation causes scar tissue to develop in the liver and nearby blood vessels, but the liver still functions normally
- cirrhosis: severe scarring from chronic inflammation, causing permanent damage, which can lead to liver failure and liver cancer.

Diagnosis

2.2 NAFLD is usually diagnosed using ultrasound. There are several non-invasive tests available to assess the stage of fibrosis in NAFLD, including blood-based tests as well as imaging such as transient elastography or acoustic radiation force impulse elastography (ARFI).

2.3 NICE's guideline on the assessment and management of non-alcoholic fatty liver disease advises to test for advanced liver fibrosis in people with NAFLD using the enhanced liver fibrosis (ELF) test. If the result of the ELF test is 10.51 or above, the NICE guideline for cirrhosis in over 16s: assessment and management recommends testing for cirrhosis using transient elastography or ARFI. Routine liver blood tests are not recommended to rule out NAFLD or test for advanced fibrosis.

2.4 The British Society of Gastroenterology (BSG) guideline on NAFLD recommends testing for fibrosis in people with NAFLD using the NAFLD fibrosis score or FIB-4. If these scores indicate an intermediate risk, transient elastography or the ELF test can be used to further clarify the diagnosis. If the non-invasive tests are not able to exclude advanced fibrosis, the BSG recommends that liver biopsy is considered to stage the level of inflammation and fibrosis, and to rule out other concomitant liver disease. Biopsy results are used to decide referral and treatment strategies for people with NAFLD. The NICE guideline for cirrhosis in over 16s: assessment and management recommends that liver biopsy is considered to diagnose cirrhosis when transient elastography is not suitable. NASH is diagnosed using biopsy. However, liver biopsy is an invasive procedure that is associated with well-recognised complications including bleeding and death. NICE's guideline on the assessment and management of non-alcoholic fatty liver disease includes a research recommendation to identify which non-invasive tests most accurately identify NASH in people with NAFLD.

Management

2.5 Treatment for NAFLD with no or minimal fibrosis consists of education on risk factors for advanced fibrosis and advice on weight management. According to the NICE guideline for non-alcoholic fatty liver disease: assessment and management, people with advanced fibrosis may be offered pioglitazone or vitamin E. There are currently no treatments available specifically for NAFLD or NASH, but people with NASH or advanced fibrosis may enter clinical trials for new therapies.

2.6 The NICE guideline for cirrhosis in over 16s: assessment and management recommends that people with cirrhosis are monitored for end-stage liver disease and liver cancer every 6 months, tested for varices, offered treatment for complications of cirrhosis (for example variceal band ligation), and potentially offered prophylactic treatment depending on comorbidities.

The interventions

LiverMultiScan

2.7 LiverMultiScan is a standalone software application produced by Perspectum that provides quantitative multiparametric analysis of non-contrast MRI. LiverMultiScan is intended to help clinicians diagnose and stage liver disease by non-invasively imaging the liver.

2.8 LiverMultiScan uses iron-corrected T1 (cT1), proton density fat fraction (PDFF) and T2* MRI protocols for its analyses. cT1 outputs are measured in milliseconds (ms), and correlate with liver fibro-inflammation. MRI PDFF is an MRI estimate of fat content and is expressed as a percentage. T2* is a measure correlated with the iron content of the liver and is used to produce the cT1 scan. The diagnosis indicated by the cT1 output and the clinical recommendations proposed by the company are as follows:

- less than 800 ms: fatty liver
  - no inflammation present
  - reassess with MRI in 3 years
- 800 ms to 875 ms: NASH
  - recommend lifestyle modification
  - manage type 2 diabetes and cardiovascular disease
  - monitor disease status with MRI after 6 months
- more than 875 ms: high-risk NASH
  - reassess with MRI every 6 months
  - consider liver biopsy if cirrhosis is suspected
  - cancer surveillance
  - consider inclusion in NASH therapeutic trials.

Magnetic resonance elastography

2.9 Magnetic resonance elastography (MRE) combines MRI with low-frequency vibrations to create a 2D or 3D elastogram showing the stiffness of tissue. In addition to the usual MRI, an external mechanical

driver passes vibrations through a flexible tube to a passive driver placed on a person's abdomen over the liver. The driver is manufactured by Resoundant. MRE is intended to generate acoustic vibrations in the body during an MRI exam to assess tissue elasticity for diagnostic purposes.

2.10 MRE is used for detecting and evaluating different stages of fibrosis and is usually added to a conventional abdominal MRI protocol. MRE outputs are provided in kilopascals (kPa). The company suggested that MRE liver stiffness outputs can be used to stage liver fibrosis as follows:

- more than 2.9 kPa: any fibrosis
- more than 3.3 kPa: significant fibrosis
- more than 3.9 kPa: advanced fibrosis
- more than 4.8 kPa: cirrhosis.

The comparator

No further testing before a decision to do a biopsy or any other care decision

2.11 Following testing as described in sections 2.2 to 2.4, in the absence of MRI-based testing, no other tests would be done before a decision to do a biopsy or any other care decision.

3 Committee discussion

The diagnostics advisory committee considered evidence on MRI-based technologies for assessing non-alcoholic fatty liver disease from several sources, including a diagnostics assessment report and an overview of that report. Full details are in the project documents for this guidance.

Reducing liver biopsies would substantially benefit patients and carers

3.1 A patient expert explained that liver biopsy has many drawbacks for people with liver disease and their carers. These include the risk of complications, needing to take time off work or education to attend the

procedure and for recovery, and the time it takes for biopsy results to be determined and communicated to people and their primary care team. MRI is much less invasive and has fewer associated risks, although some people cannot tolerate MRI scans. MRI may also not be suitable for people with a very high body mass index (BMI) because of the size of the scanner bore. The committee considered evidence from a survey (McKay et al. 2021) that reported that some people found biopsy very uncomfortable and caused psychological stress, but most found MRI to be harmless and tolerable. The committee noted that liver biopsy can also have issues such as sampling error (that is, a biopsy can only sample a small part of the liver, which may miss affected areas). The committee also noted that the risk of complications from liver biopsy is higher for people with a very high BMI, who are at higher risk of having non-alcoholic fatty liver disease (NAFLD). The committee concluded that technologies that could reduce the need for liver biopsy would be likely to substantially benefit people and carers, in terms of health and impact on their lives.

The impact of a diagnosis of NASH on clinical management is very uncertain

3.2 Perspectum, the company that manufactures LiverMultiScan, state that it should be used to distinguish non-alcoholic steatohepatitis (NASH) from simple fatty liver. Clinical experts highlighted that clinical management of NASH (if fibrosis is not detected) is generally the same as for simple fatty liver. They emphasised that the level of fibrosis or presence of cirrhosis are the main drivers of decisions about care. A clinical expert commented that if a specialist in secondary care identified a person with NASH but no fibrosis, they would discharge them back to primary care. The company stated that cT1 results are correlated with adverse outcomes in liver disease. It further commented that the potential benefit of NASH detection could be in terms of informing biopsy use, monitoring frequency and the extent of lifestyle advice offered. Clinical experts commented that the

progression of NAFLD can be slow and the impact of more frequent monitoring on earlier detection of disease progression is uncertain. They also highlighted that quality standards on managing fatty liver disease from the British Association for the Study of the Liver state that people with low risk of significant fibrosis should be reassessed in the community every 3 years. The committee acknowledged that new medicines for NASH are currently being developed and used in clinical trials, but these are not routinely used in the NHS. Routine availability of these treatments would likely increase the clinical impact of a NASH diagnosis. The committee concluded that, based on current practice, the impact of a diagnosis of NASH on clinical management is very uncertain.

Introducing MRI for people with NAFLD could have a large impact on radiology capacity

3.3 The current pathway for NAFLD does not include testing with MRI. The committee noted that introducing routine MRI testing into the care pathway for NAFLD would significantly increase demand on MRI services. Radiologist experts highlighted that wait times for MRI scans in the NHS are already long, with services working at full capacity. Introducing MRI for NAFLD would either increase waiting times for MRI (for all indications) or require further MRI capacity to be added to the NHS, including more scanners and trained staff, at considerable cost. The committee concluded that greater adoption of MRI testing for NAFLD would have a large impact on the NHS. It further concluded that the benefit of introducing MRI into the NAFLD pathway would have to be very clear to justify the impact on MRI services.

Clinical effectiveness

No test accuracy evidence was found for MRI when transient elastography or ARFI is unsuitable or has not worked

3.4 Ultrasound-based tests such as transient elastography and acoustic radiation force impulse elastography (ARFI) are typically done before liver

biopsy is considered (see sections 2.2 to 2.4). However, these tests may not be suitable for some people. This is because they have a high chance of not working if people have a high BMI, particularly with central obesity or ascites. Clinical experts considered that MRI-based tests could have particular benefit for the NHS when transient elastography or ARFI has not worked or is unsuitable. This population was identified as one of interest for this evaluation during scoping. However, no diagnostic accuracy data was found for the MRI tests in this population.

There is very little information on the impact of MRI-based tests on decisions about care

3.5 Only 1 study was identified showing the impact of an MRI-based test (LiverMultiScan) on decisions about care, specifically the level of biopsy use (see section 3.6). There was no data on the impact of magnetic resonance elastography (MRE) on decisions about care. Clinical advice to NICE during scoping was that assessment of liver health by MRI-based technologies could help motivate people with NAFLD to engage with lifestyle changes. This could help slow or even reverse progression of liver disease. No data was available to determine whether LiverMultiScan or MRE affected people's understanding of NAFLD or their adherence to lifestyle advice or interventions. People with NAFLD are likely to have overweight or obesity and it was unclear to committee the extent to which information provided by the tests would further incentivise lifestyle changes (for example, losing weight, which could have benefits beyond slowing NAFLD progression). A further suggested benefit of MRI-based tests was on decisions about monitoring frequency. The committee recalled that the NAFLD progression can be slow. The impact of more frequent monitoring on earlier detection of disease progression is uncertain (see section 3.2). No data was identified on the impact of the tests on decisions about monitoring frequency or impact of test use on earlier detection of more advanced liver disease. Clinical experts also said that MRI could be used to help with targeting a subsequent biopsy, but no

data was found on this use. People with a South Asian family background may have a more centralised distribution of body fat than the wider population, which may increase risk of NAFLD. The committee noted that the technology may be particularly beneficial for this group, but concluded that there was not enough data to support this.

Direct evidence on the effect of LiverMultiScan on biopsy use was low quality

3.6 Only RADIcAL1 (a phase 4 open-label randomised controlled trial comparing LiverMultiScan [n=403] with local standard care [n=399] in people with suspected NAFLD) gave direct evidence on the impact of MRI-based tests on decisions about care. This trial assessed the number of liver biopsies avoided by using LiverMultiScan. The study was not published, but data was available from a clinical study report provided by the company. The external assessment group (EAG) highlighted that the population in RADIcAL1 was broader than the population for this assessment. The committee noted that a relatively small number of people had a liver biopsy (55 out of 802). It further noted that the authors of the study report commented that the low number of people having biopsies was likely because there are no current treatment options for NASH. Therefore, unless the clinician suspects advanced fibrosis or cirrhosis, the clinical management will be the same for NAFLD or NASH. A lower proportion of people had 'unnecessary' biopsies (defined by the study authors as biopsy with a negative NASH result) in the LiverMultiScan trial arm (9 out of 22, 41%) compared with the standard care arm (16 out of 31, 52%), although this was not statistically significant (EAG calculated odds ratio 0.65, 95% confidence interval 0.22 to 1.96). The committee and EAG noted concerns with the quality of the study, including the low number of people who had biopsy, and the lack of information about previous testing or rationale for deciding to do a biopsy. The committee also noted that there was no information on the number of

necessary biopsies that had been missed because of the result of LiverMultiScan (see section 3.10).

No data for MRE was identified specifically in the scope population, or at specified cut-off values for advanced fibrosis or cirrhosis

3.7 The EAG's diagnostic test accuracy review included data for people with NAFLD who had not had a diagnosis of advanced fibrosis or cirrhosis. No studies were identified that assessed test accuracy in the exact populations defined during scoping: people who have indeterminate or discordant results from fibrosis testing, or when transient elastography or ARFI has not worked or is unsuitable to assess fibrosis. Clinical experts reiterated that the MRE test was likely to be most useful in populations when non-invasive tests for fibrosis (such as transient elastography) could not be used, for example because of high BMI. No diagnostic accuracy data for MRE was identified that used MRE to test for advanced fibrosis or cirrhosis using the thresholds defined by the company (3.9 kPa for advanced fibrosis, and 4.8 kPa for cirrhosis). The committee concluded that more evidence was needed for MRE in the population of interest, at the thresholds defined by the manufacturer for significant and advanced fibrosis and cirrhosis (see the section on further research).

Cost effectiveness

The disutility from missed diagnosis of liver disease is highly uncertain

3.8 In the EAG's model, liver disease that was missed by using MRI-based tests was assumed to be correctly identified 6 months later. The EAG used a value of 0.03 quality adjusted life years (QALYs) per year for the disutility associated with the liver disease that was initially missed by the tests. This disutility over the 6-month time horizon of the model had a large effect on the incremental cost-effectiveness ratio (ICER), as the QALY losses from false negative results from MRI testing were often larger than the QALY gains from avoiding liver biopsy. This meant the MRI tests caused a loss of QALYs. The source of the disutility value was

taken from the NICE guideline on non-alcoholic fatty liver disease, and was based on the difference in QALYs expected between treated and untreated NASH. The committee questioned the validity of this value. The EAG agreed and explained that it was unable to identify any alternative data to inform this parameter. Clinical experts highlighted that the progression of NAFLD can be slow and is often asymptomatic, and that the disutility accumulated over the short time horizon of the model is likely low. The EAG provided scenario analyses in which no disutility associated with missed liver disease was included in the model but cautioned that this should be considered exploratory analysis. The committee concluded that the disutility associated with a missed diagnosis of liver disease is highly uncertain.

The model potentially underestimates the costs and impact of more MRI use

3.9 The EAG's model included costs of doing MRI, but not any costs for changes to NHS infrastructure that may be needed for more MRI use. The EAG commented that the implications for NHS service provision would be significant. This is because of increased staffing levels and changes in infrastructure needed to accommodate the high demand for MRI scans for people with NAFLD. The committee recalled its conclusion that more MRI testing in NAFLD would have a significant impact on demand for MRI. This could mean purchasing more MRI scanners or increased waiting times for MRI scans (see section 3.3). The committee concluded that the true cost of introducing MRI to the care pathway for NAFLD would likely be higher than estimated in the model.

Based on current accuracy data, a confirmatory biopsy is likely to be done after a positive MRI test result

3.10 The EAG's model assumed that all people with a positive result from MRI testing would then be referred for a confirmatory biopsy. In comments submitted on the diagnostics assessment report, the companies suggested that a positive test result was sufficient for a diagnosis for

some people, and that a confirmatory biopsy was not always necessary. The EAG noted that there was no data to inform any assumption about the effect of a positive MRI test result on the clinical decision to do a biopsy. It explained that, based on clinical advice, it is appropriate to assume a confirmatory biopsy would be needed. Clinical experts commented that current data on test performance was not sufficient to be confident in a diagnosis without a biopsy. So, they would refer people with positive MRI test results for a liver biopsy. But if further data provides reassurance on test accuracy, a follow-up biopsy may not always be needed.

Time to test was not accounted for in the model

3.11 Perspectum stated that people can wait up to 18 months for a liver biopsy. It questioned whether this was incorporated in the model, noting that reducing time to testing could be an uncaptured benefit for the MRI-based tests. The EAG confirmed that this had not been included in the model. Clinical and patient experts stated that their experience of wait times for liver biopsy were much lower than suggested by the company, between 2 days and 6 months. The committee also noted that there are currently significant wait times for MRI, and that introduction of MRI to the NAFLD care pathway could further increase the wait (see section 3.3). Therefore it was not appropriate to assume that an MRI test would be done as soon as it was needed, and any quicker time to test compared with biopsy was very uncertain. A patient expert commented that if confirmatory biopsy was needed after a positive MRI test result (see section 3.10), introducing MRI could also increase the time to diagnosis compared with a pathway in which liver biopsy is done without a preceding MRI test.

LiverMultiScan was dominated or had much higher ICERs than are usually considered an acceptable use of NHS resources

3.12 Perspectum stated that LiverMultiScan was intended to distinguish NASH from NAFLD. So, the committee focused its considerations for LiverMultiScan on the cost-effectiveness estimates provided by the EAG

for NASH, advanced NASH, and high risk of progressive disease (defined as NASH or at least F2 fibrosis). In the base case, LiverMultiScan was dominated by (was more expensive and less effective than) the biopsy only pathway. This was because of the QALY losses incurred by false negative results, which the committee recalled were very uncertain (see section 3.8). This QALY loss was removed in a scenario analysis (the test no longer reduced QALYs), which improved cost effectiveness. However, the ICERs were above £118,000 per QALY gained. The EAG commented that this scenario is not plausible as it would indicate there was no impact of a correct or incorrect diagnosis, and consequently no point to testing. The EAG commented that the cost effectiveness of LiverMultiScan would be above £30,000 per QALY gained even if the test was assumed to have 100% accuracy. Threshold analyses indicated that the population prevalence of the condition being tested for would have to be much lower than found in the study by Eddowes et al. (which was used in the EAG's base case) for LiverMultiScan to be cost effective. The committee noted that the extent of decrease in biopsy use caused by LiverMultiScan use estimated by the model (up to about 30% reduction) was similar to that seen in RADIcAL1.

MRE could be cost effective, but this is highly dependent on the cost per test

3.13 Resoundant, the company that manufactures the technology used in MRE, stated that no additional cost per scan would be necessary for MRE if the hardware was already available. The EAG used 2 cost per scan estimates for MRE. The first estimate assumed that MRE was already installed, so the cost of a scan was the only cost of doing an MRI (that is, no additional cost for using MRE). Based on accuracy estimates to detect significant fibrosis (at least F2), MRE dominated (was cheaper and more effective than) the biopsy only pathway. The second estimate assumed that MRE would need to be installed and added an additional £59.50 per scan on top of the cost of doing an MRI. The EAG noted that this

additional cost was uncertain, being based on several assumptions, many of which were not evidenced. Using this cost, the ICER for detecting significant fibrosis was over £225,000 per QALY gained. Radiology experts in the committee stated that MRE is not widely available in the NHS, so the second cost-effectiveness estimate is more realistic. The EAG did not model MRE to detect advanced fibrosis (at least F3) or cirrhosis because no data was identified using the company's specified thresholds (see section 3.7). The committee also had concerns that using different costs based on whether or not a test is already available could result in inequality based on geographical location. The committee concluded that the cost of MRE was a significant factor in whether or not the test could be cost effective, and that the true cost was highly uncertain. Further clarification of the cost per person of MRE testing in the NHS would benefit future decision making.

Test accuracy data for MRE is needed in the scope population

3.14 The EAG provided cost-effectiveness estimates for MRE using data from Imajo et al. (2021). It highlighted that this population was broader than the scope population, and that a subgroup analysis based on the scope population was not possible. Clinical experts commented that MRE could have a role in the NHS if used when previous tests such as transient elastography or ARFI either could not be done, had not worked, or gave discordant results, in line with the scope population. The committee concluded that data on MRE performance is needed in populations that match the scope, either from subgroup analysis of existing studies, or further accuracy studies.

Several assumptions made in the model need further consideration once more data is available

3.15 The EAG made several assumptions in its economic model, including that:

- after an initial negative result from an MRI test (less than 875 ms), a second MRI test would be done at 6 months
- the second MRI test at 6 months was 100% accurate (that is, no liver disease remains undetected after 6 months).

Perspectum commented on the diagnostic assessment report that the pathway used in the model did not reflect its clinical advice for use of LiverMultiScan. It explained that, in line with its advice, people would only have a follow-up MRI test if their cT1 score was between 800 and 875 ms. People with a score below 800 ms would be discharged to primary care and their condition monitored every 2 to 3 years as per local guidance (see section 2.8). The EAG modelled a scenario in which people with LiverMultiScan results less than 800 ms had no further testing. ICERs remained above £200,000 per QALY gained. The EAG also noted that extending the time before a follow-up test would reduce the cost effectiveness of the MRI-based tests, as those with false negative results from the first test would accrue disutility from undiagnosed liver disease over a longer period (see section 3.8). A stakeholder also questioned the assumption that the second test done at 6 months would be 100% accurate. The EAG acknowledged that this was a simplifying assumption that favoured the MRI-based tests. The committee recalled liver biopsies can have sampling errors (see section 3.1), but that accuracy estimates used in the model were from studies that used liver biopsy as a reference standard. This may be unfavourable towards the MRI tests. The committee concluded that several assumptions used in the model would need reconsideration when more clinical data is available. This would improve the reliability of the cost-effectiveness estimates.

More accuracy data is needed to validate MRI-based test performance

3.16 There was a lack of data on test accuracy, with only 1 small study identified for LiverMultiScan that explicitly included the scope population (Eddowes et al. 2018). No studies were identified using MRE in the scope population (see section 3.7), and no studies assessed MRE using the

company-defined pre-set thresholds for advanced fibrosis or cirrhosis. The committee recalled its conclusion that the level of data available for the MRI-based tests was not high enough to replace biopsy entirely (see section 3.10). The committee concluded that the MRI-based tests need further validation compared with biopsy.

There is considerable uncertainty about how LiverMultiScan results would affect care in the NHS

3.17 Clinical experts said that there is a lack of clarity on how LiverMultiScan fits into the care pathway for NAFLD, and what care decisions the test results impact on. The clinical impact of a NASH diagnosis is uncertain (see section 3.2), and there was little evidence for the effect of LiverMultiScan results on clinical management (see section 3.5). The only available direct evidence for the impact of LiverMultiScan outputs on the number of liver biopsies was of poor quality (see section 3.6). The committee recognised that future approvals of drug treatments for NASH may make the role of LiverMultiScan and NASH diagnosis clearer. Clinical experts also commented that it is unclear how LiverMultiScan can distinguish fibrosis from inflammation. If this is not possible, a positive result could be because of either fibrosis or inflammation, and it wasn't clear how the technique could identify NASH alone. Further tests may be needed to make decisions about care. The committee concluded that there is considerable uncertainty about how LiverMultiScan results would affect care in the NHS.

4 Recommendations for further research

4.1 Further research is recommended on:

- the test accuracy of LiverMultiScan and magnetic resonance elastography (MRE) at the thresholds defined by the companies for people:
  - with indeterminate or discordant results from previous fibrosis testing

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  - when transient elastography or acoustic radiation force impulse elastography (ARFI) is unsuitable or has not worked
- the impact of LiverMultiScan and MRE test results on decisions about care, such as the decision to do a liver biopsy.

5 Implementation

NICE intends to develop tools, in association with relevant stakeholders, to help organisations put this guidance into practice.

In addition, NICE will support this guidance through a range of activities to promote the recommendations for further research. The research proposed will be considered for developing specific research study protocols as appropriate. NICE will also incorporate the research recommendations in section 4 into its guidance research recommendations database and highlight these recommendations to public research bodies.

6 Review

NICE will regularly monitor its published technology guidance to check for any new evidence or information that could affect the recommendations. Guidance will not have a fixed review date.

Mark Kroese

Chair, diagnostics advisory committee

June 2022

7 Diagnostics advisory committee members and NICE project team

Committee members

This topic was considered by the diagnostics advisory committee, which is a standing advisory committee of NICE.

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Committee members are asked to declare any interests in the test to be assessed. If it is considered there is a conflict of interest, the member is excluded from participating further in that assessment.

The minutes of each committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

Additional specialist committee members took part in the discussions for this topic:

Specialist committee members

Dr Raneem Albazaz
Consultant Radiologist, St James's University Hospital Leeds

Heather Boult
Lay specialist committee member

Dr David Breen
Associate Professor of Radiology, University Hospitals Southampton

Dr Pinelopi Manousou
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Prof Alastair O'Brien
Professor and Honorary Consultant Hepatologist, University College London Hospital and Royal Free Hospitals

Dr Jeremy Shearman
Consultant Gastroenterologist and Hepatologist, Warwick Hospital

NICE project team

Each diagnostics assessment is assigned to a team consisting of a technical analyst (who acts as the topic lead), a technical adviser and a project manager.

Jacob Grant
Topic lead

Thomas Walker

Technical adviser

Donna Barnes

Project manager (until April 2022)

Harriet Wilson

Project manager (from May 2022)

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