EAG Report: Addendum

LIVERPOOL REVIEWS AND IMPLEMENTATION GROUP (LRiG)

# MRI-based technologies for the assessment of patients with non-alcoholic fatty liver disease [DAP59]

## EAG Report: Addendum

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UNIVERSITY OF LIVERPOOL

LIVERPOOL REVIEWS AND IMPLEMENTATION GROUP

A MEMBER OF THE RUSSELL GROUP

# 1 INTRODUCTION

In this Addendum, the EAG has included the following information:

1. Text and analyses in response to NICE requests for clarification (Section 2)
2. Updated EAG report tables (correct T3 and new T8) (Section 3)

All the tables in this document include updated cT1 accuracy data used to populate diagnostic test strategy T8 (using new information provided by Perspectum Ltd). The original EAG report included T8 data based on a cT1 algorithm that is no longer used. Perspectum Ltd re-analysed the high-risk data presented in the Eddowes publication using the new algorithm to bring the high-risk data (used to populate the T8 strategy) in line with the data for the other test strategies (T1 to T7).

## *1.1 Checking for non-linearity in the model*

The EAG model is a single node decision tree and, therefore, is linear by design. Thus, exploring the impact of non-linearity by undertaking PSA is not relevant.

The NICE lead team requested that non-linearity was confirmed through increasing and decreasing model parameters by ±20%, averaging the incremental cost effectiveness ratios (ICERs per QALY gained) from these analyses and comparing them with the deterministic base case ICERs per QALY gained. The EAG performed this analysis. The results (Table 1) showed that, depending on the test strategy, the differences between the ICERs per QALY gained generated from averaging results from the ±20% analyses and the deterministic ICERs per QALY gained were between 0.01% and 0.02%.

The analysis shows that even if the EAG is wrong about the structural linearity of the model, the analyses performed show that any impact of non-linearity is not important for decision making.

Table 1 Comparison of model cost effectiveness results: deterministic versus average of ±20% of base case parameters

| Diagnostic test strategy | | LiverMultiScan Deterministic ICER per QALY | Model parameters +20% | Model parameters -20% | Average of model parameters ±20% | Average ±20% ICER minus deterministic ICER per QALY | Percentage difference |
|---|---|---|---|---|---|---|---|
| T1 | Any fibrosis (≥F1) | -£359,666 | -£363,934 | -£355,497 | -£359,715 | -£49 | 0.01% |
| T2 | Significant fibrosis (≥F2) | -£190,779 | -£193,291 | -£188,326 | -£190,809 | -£30 | 0.02% |
| T3 | Advanced fibrosis (≥F3) | -£980,001 | -£995,379 | -£964,977 | -£980,178 | -£177 | 0.02% |
| T4 | Brunt Grade ≥1 | -£148,132 | -£149,604 | -£146,694 | -£148,149 | -£17 | 0.01% |
| T5 | Brunt Grade ≥2 | £1,266,511 | £1,287,758 | £1,245,752 | £1,266,755 | -£244 | 0.02% |
| T6 | NASH (NAS≥4, ≥1 for lobular inflammation and hepatocyte ballooning) | -£381,324 | -£386,941 | -£375,835 | -£381,388 | -£65 | 0.02% |
| T7 | Advanced NASH (NAS≥4, ≥F2) | -£973,592 | -£988,866 | -£958,670 | -£973,768 | -£176 | 0.02% |
| T8 | High risk (NASH or >F1) | -£101,002 | -£102,049 | -£99,978 | -£101,013 | -£11 | 0.01% |

F=stage of fibrosis; ICER=incremental cost effectiveness ratio; NAS=non-alcoholic fatty liver disease (NAFLD) activity score; NASH=non-alcoholic steatohepatitis; QALY=quality adjusted life year

## *1.1 No use of a second LiverMultiScan for people with a result <800ms*

When considering how to reach a correct diagnosis as promptly as possible, implementing the EAG approach (i.e., constructing a model using the assumptions that (i) everyone with a negative result from an initial LMS test has a second LMS after 6 months, regardless of cT1 score, and (ii) that results from the second LMS test are always 100% accurate at 6 months), is the most optimistic scenario for the population with false negative results after an initial LMS test. However, this approach potentially also introduces the cost of a second LMS at 6 months that is unnecessary for those with true negative results from an initial LMS test.

The results provided by Eddowes/Perspectum Ltd (14th December 2021) suggested that 18.5% of patients with indeterminate results from previous fibrosis testing who are sent for biopsy have a cT1 score <800ms and 55.6% of these patients have fibrosis (F≥1). The prevalence of F≥2 and F≥3 for patients with a cT1 score<800ms could not be calculated by the EAG from the available data.

Based on Eddowes/Perspectum Ltd data, it can be determined that 47.3% of patients have a cT1 score <875ms (and will therefore have a negative result in strategies with a cT1 cut-off score of 875ms) and, of these, 39.1% will have a cT1 score<800ms. This means that, of those patients with a cT1 score<875ms, 60.9% will have a score of 800-875ms. The EAG therefore ran a scenario where, for strategies with a cut-off score of 875ms, only 60.9% of patients had a second LiverMultiScan at 6 months and where the cut-off score was 800ms, no patients had a second LiverMultiScan. In this scenario, any QALY loss from a false negative only occurs for 6 months, even if patients with a false negative result have a cT1<800ms and therefore do not have a second LiverMultiScan. A second scenario used the same retesting assumptions but removed the QALY loss for a false negative result.

Results from scenario analyses (Table 2) show that even if patients with cT1 scores <800ms do not have a second LiverMultiScan at 6 months, testing using LiverMultiScan never leads to an ICER versus no LiverMultiScan that is below £225,000 per QALY gained. This occurs using a set of assumptions that is favourable to the cost effectiveness of LiverMultiScan (i.e., patients with a cT1 score <800ms never have a second LiverMultiScan or liver biopsy and if their results are false negative do not incur a QALY loss for more than 6 months). In a scenario, where patients with a cT1<800ms do not have a second LiverMultiScan and any QALY loss from having a false negative result is removed (a scenario the ERG considers is implausibly favourable to the cost effectiveness of LiverMultiScan), the ICER per QALY gained for the comparison of testing with LiverMultiScan versus no LiverMultiScan never falls below £48,000 per QALY. The EAG, therefore, considers that the base case assumption that all patients have

a second LiverMultiScan at 6 months regardless of cT1 score does not affect the conclusions that can be drawn from the EAG base case cost effectiveness results. Further, the EAG reiterates that the EAG base case assumption that all false negatives are picked up at 6 months means that, from the perspective of LiverMultiScan, the EAG base case ICERs per QALY gained are likely to be optimistic.

Table 2 EAG scenario analyses: patients with cT1<800ms not sent for second LiverMultiScan at 6 months

| Diagnostic test strategy | | cT1 cut off score | ICER per QALY gained | | |
|---|---|---|---|---|---|
| | | | LiverMultiScan Deterministic results | Scenario 1: patients with cT1<800ms not sent for second LMS | Scenario 2: patients with cT1 <800ms not sent for second LMS AND no QALY loss for false negative results |
| T1 | Any fibrosis (≥F1) | 800ms | Dominated by no LMS | Dominated by no LMS | £587,405 |
| T2 | Significant fibrosis (≥F2) | 875ms | Dominated by no LMS | Dominated by no LMS | £73,054 |
| T3 | Advanced fibrosis (≥F3) | 875ms | Dominated by no LMS | £748,291 | £54,248 |
| T4 | Brunt Grade ≥1 | 800ms | Dominated by no LMS | Dominated by no LMS | Dominated by no LMS |
| T5 | Brunt Grade ≥2 | 875ms | £1,266,511 | £225,729 | £48,738 |
| T6 | NASH (NAS≥4, ≥1 for lobular inflammation and hepatocyte ballooning) | 875ms | Dominated by no LMS | Dominated by no LMS | £60,194 |
| T7 | Advanced NASH (NAS≥4, ≥F2) | 875ms | Dominated by no LMS | £754,729 | £54,271 |
| T8 | High risk (NASH or >F1) | 875ms | Dominated by no LMS | Dominated by no LMS | £116,081 |

cT1=iron corrected longitudinal relaxation time; EAG=External Assessment Group; F=stage of fibrosis; ICER=incremental cost effectiveness ratio; LMS=LiverMultiScan; NAS=non-alcoholic fatty liver disease (NAFLD) activity score; NASH=non-alcoholic steatohepatitis; QALY=quality adjusted life year

## *1.2 Threshold analysis for prevalence using test accuracy values*

The EAG provided a threshold analysis showing the prevalence at which a test accuracy of 100% would result in LiverMultiScan being cost effective. The NICE lead team asked for these threshold analyses to be performed using the actual test accuracy results for each testing strategy. Results from these analyses are presented in Table 3.

Table 3 EAG threshold analysis of prevalence: cost effectiveness of strategies with different QALY WTP thresholds assuming base case LiverMultiScan test accuracy

| Diagnostic test strategy | | cT1 cut-off score | Base case prevalence (Eddowes/Perspectum Ltd data) | WTP threshold: £20,000/QALY | | WTP threshold: £30,000/QALY | |
|---|---|---|---|---|---|---|---|
| | | | | Prevalence | Number of biopsies averted | Prevalence | Number of biopsies averted |
| T1 | Any fibrosis (≥F1) | 800ms | 87% | 8% | 582 | 16% | 531 |
| T2 | Significant fibrosis (≥F2) | 875ms | 65% | 13% | 617 | 18% | 581 |
| T3 | Advanced fibrosis (≥F3) | 875ms | 48% | 2% | 579 | 8% | 543 |
| T4 | Brunt Grade ≥1 | 800ms | 98% | Never | NA | Never | NA |
| T5 | Brunt Grade ≥2 | 875ms | 50% | 9% | 599 | 15% | 559 |
| T6 | NASH (NAS≥4, ≥1 for lobular inflammation and hepatocyte ballooning) | 875ms | 54% | 6% | 592 | 12% | 554 |
| T7 | Advanced NASH (NAS≥4, ≥F2) | 875ms | 48% | 2% | 578 | 8% | 543 |
| T8 | High risk (NASH or >F1) | 875ms | 83% | 21% | 657 | 24% | 625 |

cT1=iron corrected longitudinal relaxation time; EAG= External Assessment Group; F=stage of fibrosis; NA=not applicable; NAS=non-alcoholic fatty liver disease (NAFLD) activity score; NASH=non-alcoholic steatohepatitis; QALY=quality adjusted life years; WTP=willingness to pay

These threshold analyses showed that for two of the strategies, even if prevalence was zero, LiverMultiScan would not be cost effective. This is due to the low specificity of LiverMultiScan for these strategies as low specificity results in a high false positive rate. Even if LiverMultiScan is 100% sensitive and prevalence is 0% for a strategy, LiverMultiScan will not be cost effective unless the specificity is above 60%.

## *1.3 QALY loss associated with a delayed diagnosis*

The EAG has assumed a disutility associated with a false negative LMS or MRE of 0.03 per annum. This is based on the difference in utility values for treated and untreated NASH in NG49. However, the actual value of a QALY loss associated with a false negative test result is uncertain. The possible sources of QALY loss associated with a false negative test result include:

- symptomatic liver disease that develops after the false negative test result that would not have arisen following a true positive test result that led to treatment. This would include both liver disease that was present at the time of the false negative test result but was asymptomatic at that time, and symptomatic liver disease that developed after the false negative test result that may have been prevented with treatment
- any loss in life years from a delay in diagnosis of advanced liver disease or progression of liver disease that could have been prevented with a correct diagnosis (which includes any survival benefit from the additional information that would have been generated through a biopsy after a true positive test result)

On balance, as the QALY loss associated with a false negative only reflected treated versus untreated NASH, and not failure to diagnose and treat more advanced liver disease, the EAG considers that the utility value used in the model is likely to underestimate the QALY loss from a false negative test result.

The NICE lead team considers that the QALY loss resulting from a false negative LiverMultiScan result (0.03 per year) used in the EAG model could be too high for a condition that may be asymptomatic. The lead team requested a scenario analysis, for all diagnostic test strategies, in which the QALY loss from a false negative LiverMultiScan result was removed. The lead team also asked for a prevalence threshold analysis (as in Table 3) to be performed excluding the QALY loss from a false negative LiverMultiScan result. Results from these requested analyses are shown in Table 4. The EAG considers that excluding the QALY loss associated with a false negative LiverMultiScan test result, whilst providing information on the importance of this QALY loss is to overall cost effectiveness results, cannot ever be a plausible scenario. If having a false negative LiverMultiScan test result does not lead to a QALY loss, then there is no difference, in terms of QALYs, between a correct and an incorrect diagnosis. If this is the case, then there is no reason to perform a biopsy, or any of the other tests in the diagnostic pathway. The EAG considers that if patients are asymptomatic during

the 6 months prior to having the second LiverMultiScan test, the QALY loss should be interpreted as a loss in QALYs because of a delayed diagnosis. A delayed diagnosis means that the disease is more advanced at the time of diagnosis which could mean reduced treatment options, more severe symptoms and potentially reduced life expectancy. The EAG accepts the actual magnitude of the QALY loss associated with a delay in diagnosis of 6 months is unknown but considers that the assumption of no QALY loss would render the whole diagnostic pathway meaningless.

Table 4 No QALY loss from false negatives: base case ICERs per QALY gained and threshold analysis of prevalence for cost effectiveness of strategies with different QALY WTP thresholds assuming base case LMS test accuracy

| Diagnostic test strategy | | cT1 cut-off score | Base case prevalence (Eddowes/Perspectum Ltd) | ICER/ QALY | WTP threshold: £20,000/QALY | | WTP threshold: £30,000/QALY | |
|---|---|---|---|---|---|---|---|---|
| | | | | No QALY loss due to false negative LMS results | Prevalence | Number of biopsies averted | Prevalence | Number of biopsies averted |
| T1 | Any fibrosis (≥F1) | 800ms | 87% | £587,405 | 9% | 576 | 18% | 519 |
| T2 | Significant fibrosis (≥F2) | 875ms | 65% | £176,491 | 15% | 602 | 22% | 553 |
| T3 | Advanced fibrosis (≥F3) | 875ms | 48% | £118,501 | 3% | 573 | 10% | 532 |
| T4 | Brunt Grade ≥1 | 800ms | 98% | Dominated by no LMS | Never | NA | Never | NA |
| T5 | Brunt Grade ≥2 | 875ms | 50% | £103,861 | 11% | 585 | 18% | 539 |
| T6 | NASH (NAS≥4, ≥1 for lobular inflammation and hepatocyte ballooning) | 875ms | 54% | £135,392 | 7% | 586 | 15% | 536 |
| T7 | Advanced NASH (NAS≥4, ≥F2) | 875ms | 48% | £118,563 | 3% | 572 | 10% | 531 |
| T8 | High risk (NASH or >F1) | 875ms | 83% | £384,204 | 24% | 625 | 31% | 573 |

cT1=iron corrected longitudinal relaxation time; F=stage of fibrosis; ICER=incremental cost effectiveness ratio; LMS=LiverMultiScan; NA=not applicable; NAS=non-alcoholic fatty liver disease (NAFLD) activity score; NASH=non-alcoholic steatohepatitis; QALY=quality adjusted life year; WTP=willingness to pay

## *1.4 MRE analysis*

In the EAG report, an analysis for MRE was not undertaken as diagnostic test accuracy evidence for the specific population described in the final scope issued by NICE was not available. The NICE lead team asked for an analysis exploring the cost effectiveness of MRE using the diagnostic test accuracy data available for other populations.

To undertake this analysis, the EAG has used the MRE 2x2 data provided by Perspectum Ltd (14th December 2021) from the trial reported in the Imajo 2021 publication. In this trial LiverMultiScan cT1 scores and MRE were used to diagnose NASH in Japanese patients with a diagnosis or suspicion of NAFLD who were also suspected to have NASH (the ERG reiterates that this is not the population described in the final scope issued by NICE). The strategies in the EAG model where MRE 2x2 data were provided by Perspectum Ltd are shown in Table 5. All EAG MRE analyses are presented in Table 6 to Table 12.

Table 5 Sensitivity and specificity of MRE

| Diagnostic test strategy | | Magnetic resonance imaging | | | LiverMultiScan | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Cut-off | Sensitivity | Specificity | cT1 cut-off | Sensitivity | Specificity | Sensitivity | Specificity |
| | | | Perspectum Ltd/Imajo | | | Perspectum Ltd/Imajo | | Perspectum/Eddowes | |
| T1 | Any fibrosis (≥F1) | 2.9kPa | 0.79 | 1.0 | 800ms | 0.76 | 0.60 | 0.87 | 0.67 |
| T2 | Significant fibrosis (≥F2) | 3.3kPa | 0.82 | 0.83 | 875ms | 0.51 | 0.65 | 0.63 | 0.75 |
| T6 | NASH (NAS≥4, ≥1 for lobular inflammation and hepatocyte ballooning) | 3.3kPa | 0.71 | 0.41 | 875ms | 0.65 | 0.76 | 0.64 | 0.67 |
| T7 | Advanced NASH (NAS≥4, ≥F2) | 3.5kPa | 0.69 | 0.50 | 875ms | 0.65 | 0.68 | 0.64 | 0.62 |

cT1=iron corrected longitudinal relaxation time; F=stage of fibrosis; ICER=incremental cost effectiveness ratio; NAS=non-alcoholic fatty liver disease (NAFLD) activity score; NASH=non-alcoholic steatohepatitis; QALY=quality adjusted life year; WTP=willingness to pay

The ERG notes that results from a naïve between trials analysis suggest that when comparing effectiveness in the population considered by Imajo 2021 compared with the population considered by Eddowes 2018, LiverMultiScan was less accurate at diagnosing fibrosis up to and including F2 but more accurate when diagnosing NASH and advanced NASH. Whether these differences between populations exist for MRE is unclear.

Within the Imajo 2021 population, LiverMultiScan was less accurate at diagnosing fibrosis up to F2 than MRE but more accurate at diagnosing NASH than MRE, with LiverMultiScan having a slightly lower sensitivity but a markedly higher specificity than MRE for the diagnosis of advanced NASH. This suggests that for the NASH and advanced NASH testing strategies, LiverMultiScan will result in a greater reduction in unnecessary biopsies than MRE and the reverse is true for fibrosis (up to and including F2) testing strategies.

For the costs of MRE, Resoundant Inc provided information to the EAG that the approximate cost of adding MRE to an existing MRI machine would be in the region of £35,000, although new machines may add MRE for no additional cost and some centres in the UK already have MRE. The EAG has therefore estimated two costs for MRE – one assuming the MRI device already has MRE capabilities (i.e., the cost of MRE is the same as the cost of MRI alone) and the second assuming that MRE would have to be installed onto the MRI device. To estimate the cost per MRE scan if MRE has to be installed, the EAG divided the £35,000 installation cost by the estimated number of MRE scans that would be undertaken in the NICE scope population over the lifetime of the MRI machine in which MRE was installed. Currently, MRE is only used for the diagnosis of liver disease and so the use of the machine for other diseases does not need to be considered.

To estimate the number of MRE scans in the target population that would be performed over the lifetime of an MRI machine, the EAG required estimates of the:

- number of patients with NAFLD and indeterminate results from fibrosis testing in England each year
- number of MRI machines where MRE would be installed
- average lifespan of existing MRI machines in the UK.

An estimate of the number of people with NAFLD and indeterminate results from fibrosis testing in England each year is difficult to establish. The number of liver biopsies performed each year in England has been estimated to be 7,000 to 8,000 liver biopsies per year, with the majority being undertaken for the investigation of liver disease (West 2010). Not all these biopsies are for people with NAFLD with indeterminate results and include biopsies for liver cancer, hepatitis and alcoholic liver disease. The EAG has assumed that half the biopsies

were carried out in patients with NAFLD, and that half of these patients had indeterminate results from fibrosis testing. Taking the upper bound of 8,000 biopsies per year, this means that 2,000 per year could be due to patients with NAFLD and indeterminate results from fibrosis testing.

The number of MRI machines in the UK was estimated in 2017 to be 6.1 per million population (Clinical Imaging Board 2017). Applying this to the population in England of 56.5 million (Census 2021) suggests there were approximately 345 MRI machines in England in 2017. Not all MRI machines in the UK would need to be modified for MRE to meet the demand for MRE. The EAG has assumed that with only 2,000 patients per year requiring an MRE due to indeterminate results from fibrosis testing, this demand could be met if 10% of the MRI machines available were modified to perform MRE.

Results from a Royal College of Radiographers (RCR) survey (Clinical Imaging Board 2017) showed that the median age of MRI scanners in England was 7 years. The RCR quotes the European Coordination Committee of the Radiological, Electromedical and Healthcare IT Industry (COCIR) that no more than 10% of MRI machines available in a healthcare system should be aged over 10 years old. Taking these factors into account, the average remaining lifespan of MRI machines in England was estimated by the EAG as 5 years. However, if only 10% of machines were modified to perform MRE then it is reasonable to assume that only the newest machines would be modified. Thus, the EAG has assumed that the effective lifespan for an MRE modified MRI is 10 years.

These estimates can be used to generate the following results:

- the total cost of adapting 34 MRI machines so that they include MRE is £1,190,000
- the total number of patients with NAFLD and indeterminate results from testing who, over 10 years, have an MRE is 20,000
- the additional cost of MRE is £59.50, making a total cost of MRE of £207.74(the cost of a standard MRI of £148.24 + the additional cost of MRE of £59.50)

As has been detailed, this cost is built on several assumptions, some of which are not evidenced. Therefore, as was the case for the EAG analysis of LiverMultiScan, the EAG has carried out threshold analyses to determine the price of MRE at which MRE would be cost effective at WTP thresholds of £20,000 and £30,000 per QALY gained.

The proportion of failed MRE tests was assumed to be identical to the proportion of failed LiverMultiScan tests. The EAG has also used the assumption that was used to generate LiverMultiScan base case results, i.e., all patients with a negative result from a MRE are recalled at 6 months for a second MRE, at which point a correct diagnosis is made.

Table 6 Initial MRE outcomes generated by the EAG model (per 1,000 tests)

| Diagnostic test strategy | | Cut-off score | True positive | True negative | False positive | False negative | Failed tests |
|---|---|---|---|---|---|---|---|
| T1 | Any fibrosis (≥F1) | 2.9kPa | 649.5 | 122.9 | 0.0 | 172.7 | 55.0 |
| T2 | Significant fibrosis (≥F2) | 3.3kPa | 505.2 | 273.0 | 55.9 | 110.9 | 55.0 |
| T6 | NASH (NAS≥4, ≥1 for lobular inflammation and hepatocyte ballooning) | 3.0kPa | 365.0 | 176.7 | 254.2 | 149.1 | 55.0 |
| T7 | Advanced NASH (NAS≥4 plus ≥F2) | 3.5kPa | 311.7 | 246.6 | 246.6 | 140.0 | 55.0 |

EAG=External Assessment Group; F=stage of fibrosis; MRE=magnetic resonance elastography; NAS=non-alcoholic fatty liver disease (NAFLD) activity score; NASH=non-alcoholic steatohepatitis

Table 7 MRE plus biopsy pathway: biopsies performed and averted (per 1,000 patients)

| Diagnostic test strategy | | Cut-off score | Total number of biopsies, including those following a repeated MRE at 6 months | Biopsies averted | Unnecessary biopsies |
|---|---|---|---|---|---|
| T1 | Any fibrosis (≥F1) | 2.9kPa | 877.2 | 122.9 | 7.2 |
| T2 | Significant fibrosis (≥F2) | 3.3kPa | 727.0 | 273.0 | 75.0 |
| T6 | NASH (NAS≥4, ≥1 for lobular inflammation and hepatocyte ballooning) | 3.3kPa | 823.3 | 176.7 | 279.3 |
| T7 | Advanced NASH (NAS≥4 plus ≥F2) | 3.5kPa | 753.4 | 246.6 | 275.4 |

F=stage of fibrosis; MRE=magnetic resonance elastography; NAS=non-alcoholic fatty liver disease (NAFLD) activity score; NASH=non-alcoholic steatohepatitis

Table 8 Pathway diagnostic test strategy costs (per 1,000 patients) – MRE cost of £59.50 on top of MRI cost

| Diagnostic test strategy | | MRE cut-off score | MRE plus biopsy pathway costs | | | | Biopsy only pathway costs | | | Additional cost for the MRE pathway |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Biopsy procedures | Biopsy complications | MRE | Total costs | Biopsy procedures | Biopsy complications | Total costs | |
| T1 | Any fibrosis (≥F1) | 2.9kPa | £706,106 | £7,491 | £269,127 | £982,724 | £805,000 | £8,540 | £813,540 | £169,184 |
| T2 | Significant fibrosis (≥F2) | 3.3kPa | £585,272 | £6,209 | £287,483 | £878,964 | £805,000 | £8,540 | £813,540 | £65,424 |
| T6 | NASH (NAS≥4, ≥1 for lobular inflammation and hepatocyte ballooning) | 3.3kPa | £662,775 | £7,031 | £275,413 | £945,219 | £805,000 | £8,540 | £813,540 | £131,679 |
| T7 | Advanced NASH (NAS≥4 plus ≥F2) | 3.5kPa | £606,451 | £6,434 | £288,068 | £900,952 | £805,000 | £8,540 | £813,540 | £87,412 |

F=stage of fibrosis; MRE=magnetic resonance elastography; NAS=non-alcoholic fatty liver disease (NAFLD) activity score; NASH=non-alcoholic steatohepatitis

Table 9 Pathway diagnostic test strategy costs (per 1,000 patients) – no MRE cost in addition to MRI cost

| Diagnostic test strategy | | MRE cut-off score | MRE plus biopsy pathway costs | | | | Biopsy only pathway costs | | | Additional cost for the MRE pathway |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Biopsy procedures | Biopsy complications | MRE | Total costs | Biopsy procedures | Biopsy complications | Total costs | |
| T1 | Any fibrosis (≥F1) | 2.9kPa | £706,106 | £7,491 | £192,045 | £905,642 | £805,000 | £8,540 | £813,540 | £92,102 |
| T2 | Significant fibrosis (≥F2) | 3.3kPa | £585,272 | £6,209 | £205,143 | £796,624 | £805,000 | £8,540 | £813,540 | -£16,916 |
| T6 | NASH (NAS≥4, ≥1 for lobular inflammation and hepatocyte ballooning) | 3.3kPa | £662,775 | £7,031 | £196,531 | £866,337 | £805,000 | £8,540 | £813,540 | £52,797 |
| T7 | Advanced NASH (NAS≥4 plus ≥F2) | 3.5kPa | £606,451 | £6,434 | £205,561 | £818,445 | £805,000 | £8,540 | £813,540 | £4,905 |

F=stage of fibrosis; MRE=magnetic resonance elastography; NAS=non-alcoholic fatty liver disease (NAFLD) activity score; NASH=non-alcoholic steatohepatitis

Table 10 QALY analyses for the two diagnostic pathways (per 1,000 patients)

| Diagnostic test strategy | | MRE cut-off score | MRE plus biopsy pathway | | | | | Biopsy only pathway | | | | Incremental QALYs (MRE+biopsy pathway)* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Biopsy procedure | Biopsy complications | Biopsy death | False negatives | Total QALY losses | Biopsy procedure | Biopsy complications | Biopsy death | Total QALY losses | |
| T1 | Any fibrosis (≥F1) | 2.9kPa | 4.89 | 0.13 | 1.24 | 2.59 | 8.85 | 5.58 | 0.15 | 1.41 | 7.14 | -1.71 |
| T2 | Significant fibrosis (≥F2) | 3.3kPa | 4.06 | 0.11 | 1.03 | 1.66 | 6.85 | 5.58 | 0.15 | 1.41 | 7.14 | 0.28 |
| T6 | NASH (NAS≥4, ≥1 for lobular inflammation and hepatocyte ballooning) | 3.3kPa | 4.59 | 0.12 | 1.16 | 2.24 | 8.11 | 5.58 | 0.15 | 1.41 | 7.14 | -0.98 |
| T7 | Advanced NASH (NAS≥4 plus ≥F2) | 3.5kPa | 4.20 | 0.11 | 1.06 | 2.10 | 7.48 | 5.58 | 0.15 | 1.41 | 7.14 | -0.34 |

* A negative value means that the biopsy only pathway generates more QALYs than the MRE+biopsy pathway; a positive value means that the MRE plus biopsy pathway generates more QALYs than the biopsy only pathway

F=stage of fibrosis; MRE=magnetic resonance elastography; NAS=non-alcoholic fatty liver disease (NAFLD) activity score; NASH=non-alcoholic steatohepatitis; QALY=quality adjusted life year

Table 11 Incremental analyses for MRE plus biopsy versus biopsy (1,000 patients) – MRE cost of £59.50 on top of MRI cost

| Diagnostic test strategy | | MRE cut-off score | QALY loss from false negatives | | | No QALY loss from false negatives | | |
|---|---|---|---|---|---|---|---|---|
| | | | Incremental | | ICER per QALY gained (versus biopsy) | Incremental | | ICER per QALY gained (versus biopsy) |
| | | | Costs | QALYs | | Costs | QALYs | |
| T1 | Any fibrosis (≥F1) | 2.9kPa | £169,184 | -1.71 | MRE+biopsy dominated by biopsy | £169,184 | 0.88 | £192,961 |
| T2 | Significant fibrosis (≥F2) | 3.3kPa | £65,424 | 0.28 | £229,967 | £65,424 | 1.95 | £33,584 |
| T6 | NASH (NAS≥4, ≥1 for lobular inflammation and hepatocyte ballooning) | 3.3kPa | £131,679 | -0.98 | MRE+biopsy dominated by biopsy | £131,679 | 1.26 | £104,429 |
| T7 | Advanced NASH (NAS≥4 plus ≥F2) | 3.5kPa | £87,412 | -0.34 | MRE+biopsy dominated by biopsy | £87,412 | 1.76 | £49,657 |

F=stage of fibrosis; ICER=incremental cost effectiveness ratio; MRE=magnetic resonance elastography; NAS=non-alcoholic fatty liver disease (NAFLD) activity score; NASH=non-alcoholic steatohepatitis; QALY=quality adjusted life year

Table 12 Incremental analyses for MRE plus biopsy versus biopsy (1,000 patients) – no MRE cost on top of MRI cost

| Diagnostic test strategy | | MRE cut-off score | QALY loss from false negatives | | | No QALY loss from false negatives | | |
|---|---|---|---|---|---|---|---|---|
| | | | Incremental | | ICER per QALY gained (versus biopsy) | Incremental | | ICER per QALY gained (versus biopsy) |
| | | | Costs | QALYs | | Costs | QALYs | |
| T1 | Any fibrosis (≥F1) | 2.9kPa | £92,102 | -1.71 | MRE+biopsy dominated by biopsy | £92,102 | 0.88 | £105,045 |
| T2 | Significant fibrosis (≥F2) | 3.3kPa | -£16,916 | 0.28 | MRE+biopsy **dominates** biopsy | -£16,916 | 1.95 | MRE+biopsy dominates biopsy |
| T6 | NASH (NAS≥4, ≥1 for lobular inflammation and hepatocyte ballooning) | 3.3kPa | £52,797 | -0.98 | MRE+biopsy dominated by biopsy | £52,797 | 1.26 | £41,871 |
| T7 | Advanced NASH (NAS≥4 plus ≥F2) | 3.5kPa | £4,905 | -0.34 | MRE+biopsy dominated by biopsy | £4,905 | 1.76 | £2,787 |

F=stage of fibrosis; ICER=incremental cost effectiveness ratio; MRE=magnetic resonance elastography; NAS=non-alcoholic fatty liver disease (NAFLD) activity score; NASH=non-alcoholic steatohepatitis; QALY=quality adjusted life year

In addition to base case analyses, the EAG undertook threshold analysis to determine at what prevalence and total cost the different MRE testing strategies would become cost effective at £20,000 and £30,000 (Table 13). Results without any additional cost of MRE over a standard MRI are provided in

Table 14.

The EAG reiterates that results from all MRE analyses should be interpreted with caution. The MRE effectiveness evidence has not been sourced from the target population and the overall analyses are still, in the opinion of the EAG, likely to generate optimistic QALY gains for MRI (LiverMultiScan or MRE) over no MRI. Interpreting the results with these caveats, MRE is unlikely to be cost effective at a WTP of £20,000 or £30,000 per QALY if there is a QALY loss associated with false negative test results or if there is an additional cost of MRE above that of the cost of MRI. If there is no or minimal QALY loss associated with false negatives and MRE adds no additional costs to MRI then, potentially, testing for advanced NASH or significant fibrosis with MRE whilst only undertaking a biopsy in patients who have positive test results, may be cost effective.

Table 13 MRE plus biopsy versus biopsy (1,000 patients) – prevalence and total MRE cost at which MRE becomes cost effective at different QALY WTP thresholds

| Diagnostic test strategy | | MRE cut-off score | Base case prevalence from CALM trial | £20,000/QALY | | | £30,000/QALY | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Prevalence (QALY loss from false negative) | Prevalence (no QALY loss from false negative) | Price of MRE at which it becomes cost effective | Prevalence (QALY loss from false negative) | Prevalence (no QALY loss from false negative) | Price of MRE at which it becomes cost effective |
| T1 | Any fibrosis (≥F1) | 2.9kPa | 87% | 62% | 67% | £50.70* | 63% | 69% | £37.48* |
| T2 | Significant fibrosis (≥F2) | 3.3kPa | 65% | 56% | 61% | £164.58 | 58% | 64% | £166.63 |
| T6 | NASH (NAS≥4, ≥1 for lobular inflammation and hepatocyte ballooning) | 3.3kPa | 54% | 19% | 24% | £93.70* | 22% | 29% | £86.35* |
| T7 | Advanced NASH (NAS≥4 plus ≥F2) | 3.5kPa | 48% | 29% | 35% | £139.80* | 31% | 40% | £137.34* |

*The ICERs in these scenarios are in the south-west quadrant and as such lower costs for MRE are required to make the QALY loss associated with each strategy compared to no MRE cost effective as the WTP threshold increases from £20,000 to £30,000 per QALY

F=stage of fibrosis; MRE=magnetic resonance elastography; NAS=non-alcoholic fatty liver disease (NAFLD) activity score; NASH=non-alcoholic steatohepatitis; QALY=quality adjusted life year; WTP=willingness to pay

Table 14 MRE plus biopsy versus biopsy (1,000 patients) – prevalence at which MRE becomes cost effective at different QALY WTP thresholds with no additional cost per MRE over a standard MRI

| Diagnostic test strategy | | MRE cut-off score | Base case prevalence from CALM trial | £20,000/QALY | | £30,000/QALY | |
|---|---|---|---|---|---|---|---|
| | | | | Prevalence (QALY loss from false negative) | Prevalence (no QALY loss from false negative) | Prevalence (QALY loss from false negative) | Prevalence (no QALY loss from false negative) |
| T1 | Any fibrosis (≥F1) | 2.9kPa | 87% | 72% | 78% | 72% | 79% |
| T2 | Significant fibrosis (≥F2) | 3.3kPa | 65% | MRE+biopsy dominates biopsy | | | |
| T6 | NASH (NAS≥4, ≥1 for lobular inflammation and hepatocyte ballooning) | 3.3kPa | 54% | 19% | 47% | 22% | 50% |
| T7 | Advanced NASH (NAS≥4 plus ≥F2) | 3.5kPa | 48% | 46% | 55% | 45% | 58% |

F=stage of fibrosis; MRE=magnetic resonance elastography; NAS=non-alcoholic fatty liver disease (NAFLD) activity score; NASH=non-alcoholic steatohepatitis; QALY=quality adjusted life year; WTP=willingness to pay

# 2 UPDATED ORIGINAL EAG REPORT TABLES

These tables have been generated using the new T8 values (and the correct T3 values).

Table 15 LiverMultiScan diagnostic test accuracy strategies and values (per 1,000 successful tests)*

| Diagnostic test strategy | | cT1 cut-off value | Population prevalence | True positive | True negative | False positive | False negative | Sensitivity | Specificity |
|---|---|---|---|---|---|---|---|---|---|
| T1 | Any fibrosis (≥F1) | 800ms | 87.0% | 761 | 87 | 43 | 109 | 0.88 | 0.67 |
| T2 | Significant fibrosis (≥F2) | 875ms | 65.2% | 413 | 261 | 87 | 239 | 0.63 | 0.75 |
| T3 | Advanced fibrosis (≥F3) | 875ms | 47.8% | 304 | 326 | 196 | 174 | 0.64 | 0.63 |
| T4 | Brunt Grade ≥1 | 800ms | 97.8% | 782 | 0 | 22 | 196 | 0.8 | 0 |
| T5 | Brunt Grade ≥2 | 875ms | 50.0% | 348 | 348 | 152 | 152 | 0.7 | 0.7 |
| T6 | NASH (NAS≥4, ≥1 for lobular inflammation and hepatocyte ballooning) | 875ms | 54.4% | 348 | 304 | 152 | 196 | 0.64 | 0.67 |
| T7 | Advanced NASH (NAS≥4 plus ≥F2) | 875ms | 47.8% | 304 | 326 | 196 | 174 | 0.64 | 0.62 |
| T8 | High risk (NASH or >F1) | 875ms | 82.6% | 478 | 152 | 22 | 348 | 0.58 | 0.88 |

* This table includes corrected T3 values and updated T8 values
cT1= iron corrected longitudinal relaxation time; DTA=diagnostic test accuracy; F=fibrosis stage; NAS=non-alcoholic fatty liver disease (NAFLD) activity score; NASH=non-alcoholic steatohepatitis
Source: Eddowes 2018 study/Perspectum Ltd[29,71]

Table 16 EAG base case model assumptions*

| Parameter | Assumption | Source/justification |
|---|---|---|
| Percentage of patients with a positive LiverMultiScan who go to biopsy | 100% | Clinical advice |
| Percentage of patients with FN results who are retested and correctly diagnosed at 6 months | 100% | Conservative assumption that would favour LiverMultiScan (i.e., produce optimistic ICERs per QALY gained for the use of LiverMultiScan) |
| Time horizon | 6 months | Sufficient to capture key differences in costs and benefits between LiverMultiScan plus biopsy and a biopsy only pathways |
| Discount rate | NA | As model time horizon was under 12 months, no discounting was included in the model |
| **Population prevalence** | | |
| T1: Any fibrosis (≥F1) | 87.0% | Eddowes 2018/Perspectum Ltd[29,71] |
| T2: Significant fibrosis (≥F2) | 65.2% | |
| T3: Advanced fibrosis (≥F3) | 47.8% | |
| T4: Brunt Grade ≥1 | 97.8% | |
| T5: Brunt Grade ≥2 | 50.0% | |
| T6: NASH (NAS≥4, ≥1 for lobular inflammation and hepatocyte ballooning) | 54.4% | |
| T7: Advanced NASH (NAS≥4 plus ≥F2) | 47.8% | |
| T8: High risk (NASH or >F1) | 82.6% | |
| **LiverMultiScan Test Accuracy** | | |
| ***Sensitivity*** | | |
| T1: Any fibrosis (≥F1) | 0.88 | Eddowes 2018/Perspectum Ltd[29,71] |
| T2: Significant fibrosis (≥F2) | 0.63 | |
| T3: Advanced fibrosis (≥F3) | 0.64 | |
| T4: Brunt Grade ≥1 | 0.8 | |
| T5: Brunt Grade ≥2 | 0.7 | |
| T6: NASH (NAS≥4, ≥1 for lobular inflammation and hepatocyte | 0.64 | |

| | | |
|---|---|---|
| ballooning) | | |
| T7: Advanced NASH (NAS≥4 plus ≥F2) | 0.64 | |
| T8: High risk (NASH or >F1) | 0.58 | |
| ***Specificity*** | | |
| T1: Any fibrosis (≥F1) | 0.67 | Eddowes 2018/Perspectum Ltd[29,71] |
| T2: Significant fibrosis (≥F2) | 0.75 | |
| T3: Advanced fibrosis (≥F3) | 0.63 | |
| T4: Brunt Grade ≥1 | 0 | |
| T5: Brunt Grade ≥2 | 0.7 | |
| T6: NASH (NAS≥4, ≥1 for lobular inflammation and hepatocyte ballooning) | 0.67 | |
| T7: Advanced NASH (NAS≥4 plus ≥F2) | 0.62 | |
| T8: High risk (NASH or >F1) | 0.88 | |
| **Costs** | | |
| Biopsy | £805 | Weighted average of YG10Z Percutaneous transvascular biopsy of lesion of liver and YG11A Percutaneous punch biopsy of lesion of liver, 19 years and over from NHS Reference Costs[79] |
| MRI | £148.24 | RD01A Scan of one area, without contrast, 19 years and over from NHS Reference Costs[79] |
| LiverMultiScan | £199 | Cost per scan for data analysis and reporting provided by Perspectum Ltd[71] |
| **Utilities** | | |
| ***QALY losses associated with having a liver biopsy*** | | |
| Direct pain and anxiety | 0.00453 | Assumption based upon clinical advice |
| Serious adverse events | 0.000147 | Sourced from literature |
| Death | 0.00141 | Assumption based upon risk of death from biopsy |
| ***Other QALY losses*** | | |
| QALY loss from failure to treat advanced liver disease | 0.03 pa | QALY loss from untreated NASH from NG49[9] |

* This table includes corrected T3 values and updated T8 values
F=stage of fibrosis; FN=false negative; ICER=incremental cost effectiveness ratio; MRI=magnetic resonance imaging; NA=not applicable; NAS=non-alcoholic fatty liver disease (NAFLD) activity score; NASH=non-alcoholic steatohepatitis; NG=NICE guideline; QALY=quality adjusted life year

Table 17 Initial LiverMultiScan outcomes generated by the EAG model (per 1,000 tests)*

| Diagnostic test strategy | cT1 cut-off value | True Positive | True Negative | False Positive | False Negative | Failed tests |
|---|---|---|---|---|---|---|
| T1: Any fibrosis (≥F1) | 800ms | 719.1 | 82.2 | 40.6 | 103.0 | 55.0 |
| T2: Significant fibrosis (≥F2) | 875ms | 390.3 | 246.6 | 82.2 | 225.9 | 55.0 |
| T3: Advanced fibrosis (≥F3) | 875ms | 287.6 | 308.2 | 184.9 | 164.3 | 55.0 |
| T4: Brunt Grade ≥1 | 800ms | 739.9 | 0.0 | 20.8 | 185.2 | 55.0 |
| T5: Brunt Grade ≥2 | 875ms | 328.9 | 328.9 | 143.6 | 143.6 | 55.0 |
| T6: NASH (NAS≥4, ≥1 for lobular inflammation and hepatocyte ballooning) | 875ms | 328.9 | 287.3 | 143.6 | 185.2 | 55.0 |
| T7: Advanced NASH (NAS≥4 plus ≥F2) | 875ms | 287.3 | 308.1 | 185.2 | 164.4 | 55.0 |
| T8: High Risk (NASH or >F1) | 875ms | 452.0 | 143.8 | 20.5 | 328.7 | 55.0 |

* This table includes corrected T3 values and updated T8 values
cT1=iron corrected longitudinal relaxation time; EAG=External Assessment Group; F=stage of fibrosis; NAS=non-alcoholic fatty liver disease (NAFLD) activity score; NASH=non-alcoholic steatohepatitis

Table 18 LiverMultiScan plus biopsy pathway: biopsies performed and averted (per 1,000 patients)*

| Diagnostic test strategy | cT1 cut-off value | Total number of biopsies, including those following a repeated LiverMultiScan at 6 months | Biopsies averted |
|---|---|---|---|
| T1: Any fibrosis (≥F1) | 800ms | 917.8 | 82.2 |
| T2: Significant fibrosis (≥F2) | 875ms | 753.4 | 246.6 |
| T3: Advanced fibrosis (≥F3) | 875ms | 691.8 | 308.2 |
| T4: Brunt Grade ≥1 | 800ms | 1000 | 0.0 |
| T5: Brunt Grade ≥2 | 875ms | 671.1 | 328.9 |
| T6: NASH (NAS≥4, ≥1 for lobular inflammation and hepatocyte ballooning) | 875ms | 712.7 | 287.3 |
| T7: Advanced NASH (NAS≥4 plus ≥F2) | 875ms | 691.9 | 308.1 |
| T8: High Risk (NASH or >F1) | 875ms | 898.9 | 143.8 |

* This table includes corrected T3 values and updated T8 values
cT1=iron corrected longitudinal relaxation time; F=stage of fibrosis; MRI=magnetic resonance imaging; NAS=non-alcoholic fatty liver disease (NAFLD) activity score; NASH=non-alcoholic steatohepatitis

Table 19 Pathway diagnostic test strategy costs (per 1,000 patients)*

| Diagnostic test strategy | cT1 cut-off value | LiverMultiScan plus biopsy pathway costs | | | | Biopsy only pathway costs | | | Additional cost for the LMS pathway |
|---|---|---|---|---|---|---|---|---|---|
| | | Biopsy procedures | Biopsy complications | LiverMultiScan test | Total costs | Biopsy procedures | Biopsy complications | Total costs | |
| T1: Any fibrosis (≥F1) | 800ms | £738,817 | £7,838 | £411,556 | £1,158,211 | £805,000 | £8,540 | £813,540 | £344,671 |
| T2: Significant fibrosis (≥F2) | 875ms | £606,451 | £6,434 | £511,311 | £1,124,195 | £805,000 | £8,540 | £813,540 | £310,655 |
| T3: Advanced fibrosis (≥F3) | 875ms | £556,938 | £5,908 | £511,311 | £1,074,157 | £805,000 | £8,540 | £813,540 | £260,617 |
| T4: Brunt Grade ≥1 | 800ms | £805,000 | £8,540 | £411,556 | £1,225,096 | £805,000 | £8,540 | £813,540 | £411,556 |
| T5: Brunt Grade ≥2 | 875ms | £540,268 | £5,732 | £511,311 | £1,057,310 | £805,000 | £8,540 | £813,540 | £243,770 |
| T6: NASH (NAS≥4, ≥1 for lobular inflammation and hepatocyte ballooning) | 875ms | £573,740 | £6,087 | £511,311 | £1,091,137 | £805,000 | £8,540 | £813,540 | £277,597 |
| T7: Advanced NASH (NAS≥4 plus ≥F2) | 875ms | £557,004 | £5,909 | £511,311 | £1,074,224 | £805,000 | £8,540 | £813,540 | £260,684 |
| T8: High Risk (NASH or >F1) | 875ms | £689,238 | £7,312 | £511,311 | £1,207,860 | £805,000 | £8,540 | £813,540 | £394,320 |

* This table includes corrected T3 values and updated T8 values

cT1=iron corrected longitudinal relaxation time; F=stage of fibrosis; LMS=LiverMultiScan; NAS=non-alcoholic fatty liver disease (NAFLD) activity score; NASH=non-alcoholic steatohepatitis

Table 20 QALY analyses for the two diagnostic pathways (per 1,000 patients)*

| Diagnostic test strategy | cT1 cut-off value | LiverMultiScan plus biopsy pathway | | | | | Biopsy only pathway | | | | Incremental QALYs (LMS+biopsy pathway)** |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Biopsy procedure | Biopsy complications | Biopsy death | False negatives | Total QALY losses | Biopsy procedure | Biopsy complications | Biopsy death | Total QALY losses | |
| T1: Any fibrosis (≥F1) | 800ms | 5.12 | 0.13 | 1.29 | 1.55 | 8.10 | 5.58 | 0.15 | 1.41 | 7.14 | -0.96 |
| T2: Significant fibrosis (≥F2) | 875ms | 4.20 | 0.11 | 1.06 | 3.39 | 8.76 | 5.58 | 0.15 | 1.41 | 7.14 | -1.63 |
| T3: Advanced fibrosis (≥F3) | 875ms | 3.86 | 0.10 | 0.98 | 2.47 | 7.40 | 5.58 | 0.15 | 1.41 | 7.14 | -0.27 |
| T4: Brunt Grade ≥1 | 800ms | 5.58 | 0.15 | 1.41 | 2.78 | 9.92 | 5.58 | 0.15 | 1.41 | 7.14 | -2.78 |
| T5: Brunt Grade ≥2 | 875ms | 3.74 | 0.10 | 0.95 | 2.15 | 6.94 | 5.58 | 0.15 | 1.41 | 7.14 | 0.19 |
| T6: NASH (NAS≥4, ≥1 for lobular inflammation and hepatocyte ballooning) | 875ms | 3.98 | 0.10 | 1.00 | 2.78 | 7.86 | 5.58 | 0.15 | 1.41 | 7.14 | -0.73 |
| T7: Advanced NASH (NAS≥4 plus ≥F2) | 875ms | 3.86 | 0.10 | 0.98 | 2.47 | 7.40 | 5.58 | 0.15 | 1.41 | 7.14 | -0.27 |
| T8: High risk (NASH or >F1) | 875ms | 4.78 | 0.13 | 1.21 | 4.93 | 11.04 | 5.58 | 0.15 | 1.41 | 7.14 | -3.90 |

* This table includes corrected T3 values and updated T8 values

** A negative value means that the biopsy only pathway generates more QALYs than LMS+biopsy pathway; a positive value means that the LiverMultiScan plus biopsy pathway generates more QALYs than biopsy only pathway

cT1=iron corrected longitudinal relaxation time; F=stage of fibrosis; LMS=LiverMultiScan; NAS=non-alcoholic fatty liver disease (NAFLD) activity score; NASH=non-alcoholic steatohepatitis; QALY=quality adjusted life year

Table 21 Incremental analyses for LiverMultiScan plus biopsy versus biopsy (1,000 patients)*

| Diagnostic test strategy | cT1 cut-off value | Incremental | | ICER per QALY gained (versus biopsy) |
|---|---|---|---|---|
| | | Costs | QALYs | |
| T1: Any fibrosis (≥F1) | 800ms | £344,671 | -0.96 | LMS+biopsy dominated by biopsy |
| T2: Significant fibrosis (≥F2) | 875ms | £310,655 | -1.63 | LMS+biopsy dominated by biopsy |
| T3: Advanced fibrosis (≥F3) | 875ms | £260,617 | -0.27 | LMS+biopsy dominated by biopsy |
| T4: Brunt Grade ≥1 | 800ms | £411,556 | -2.78 | LMS+biopsy dominated by biopsy |
| T5: Brunt Grade ≥2 | 875ms | £243,770 | 0.19 | £1,266,511 |
| T6: NASH (NAS≥4, ≥1 for lobular inflammation and hepatocyte ballooning) | 875ms | £277,597 | -0.73 | LMS+biopsy dominated by biopsy |
| T7: Advanced NASH (NAS≥4 plus ≥F2) | 875ms | £260,684 | -0.27 | LMS+biopsy dominated by biopsy |
| T8: High risk (NASH or >F1) | 875ms | £394,320 | -3.90 | LMS+biopsy dominated by biopsy |

* This table includes corrected T3 values and updated T8 values
cT1=iron corrected longitudinal relaxation time; F=stage of fibrosis; NAS=non-alcoholic fatty liver disease (NAFLD) activity score; NASH=non-alcoholic steatohepatitis; QALY=quality adjusted life year

Table 22 QALY loss associated with biopsy: results from threshold analyses*

| Diagnostic test strategy | Threshold: £20,000 per QALY | | | Threshold: £30,000 per QALY | | |
|---|---|---|---|---|---|---|
| | Original QALY loss | Threshold QALY loss | Increase from original | Original QALY loss | Threshold QALY loss | Increase from original |
| T5: Brunt Grade ≥2 | 0.007 | 0.044 | 514% | 0.007 | 0.031 | 340% |

* This table includes updated T8 values
NAS=non-alcoholic fatty liver disease (NAFLD) activity score; NASH=non-alcoholic steatohepatitis; ICER=incremental cost effectiveness ratio; QALY=quality adjusted life year

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