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LiverMultiScan as an alternative to liver biopsy to monitor autoimmune hepatitis in the National Health Service in England: an economic evaluation

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ABSTRACT

Background Autoimmune hepatitis (AIH) is a rare chronic progressive liver disease, managed with corticosteroids and immunosuppressants and monitored using a combination of liver biochemistry and histology. Liver biopsy (gold standard) is invasive, costly and has risk of complications. Non-invasive imaging using multiparametric magnetic resonance (mpMR) can detect the presence and extent of hepatic fibroinflammation in a risk-free manner.

Objective To conduct early economic modelling to assess the affordability of using mpMR as an alternative to liver biopsy.

Methods Medical test costs associated with following 100 patients over a 5-year time horizon were assessed from a National Health Service payor perspective using tariff costs and average biopsy-related adverse events costs. Sensitivity analyses modelling the cost consequences of increasing the frequency of mpMR monitoring within the fixed cost of liver biopsy were performed.

Results Per 100 moderate/severe AIH patients receiving an annual mpMR scan (in place of biopsy), early economic modelling showed minimum cost savings of £232 333. Per 100 mild/moderate AIH patients receiving three mpMR scans over 5 years estimated minimum cost savings were £139 400. One-way sensitivity analyses showed increasing the frequency of mpMR scans from 5 to 10 over 5 years in moderate/severe AIH patients results in a cost saving of £121 926.20. In patients with mild/moderate AIH, an increase from 3 to 6 mpMR scans over 5 years could save £73 155.72. In a minimalistic approach, the use of 5 mpMR scans was still cost saving (£5770.48) if they were to replace two biopsies over the 5-year period for all patients with moderate/severe or mild/moderate AIH.

Conclusions Integration of mpMR scans in AIH patient pathways leads to significant cost savings when liver biopsy frequency is either reduced or eliminated, in addition to improved patient experience and clinician acceptability as well as providing detailed phenotyping to improve patient outcomes.

Trial registration NCT03979053.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ First early economic evaluation of cost comparison using sensitivity analysis modelling increasing the occurrence of non-invasive assessment within the fixed cost of liver biopsy.
⇒ Primary evidence of feasibility and effectiveness of using multiparametric MRI will be established using decision-analytic hypothetical model using National Health Service tariff costs (NHS 2019/2020 tariff).
⇒ Heterogeneity in liver biopsy frequency varies the costs associated with real-world patient management.
⇒ Base case modelling assumed zero cure rates.

INTRODUCTION

Autoimmune hepatitis (AIH) is a rare chronic liver disease with a prevalence of 34.04 per 100 000,[1] affecting approximately 10 000 people in the UK.[2] Patients with AIH are managed with corticosteroids and immunosuppressive regimens with the goals of improving symptoms and halting inflammation and disease progression. Disease relapse/flare occurs in the majority of patients over the time course of their disease.[2 3] Clinical guidelines recommend the use of liver biopsy to stage and assess inflammation and fibrosis, as well as to exclude alternative/comorbid aetiologies at diagnosis and during disease monitoring at times of disease flares and/or at disease remission when considering withdrawal of immunosuppression.[2] However, liver biopsy is an invasive procedure that is unpopular with patients and carries a risk of complications.[4] It is also associated with potential for sampling error and high interobserver variability.[5–8] Serum liver enzymes, such as alanine aminotransferase and aspartate aminotransferase are used to inform clinical management. However, their normalisation does not always exclude underlying residual hepatic inflammation.[9–12]

Liver*MultiScan* is a non-invasive diagnostic technology, not requiring the purchase of any additional physical kit, that postprocesses

non-contrast multiparametric magnetic resonance (mpMR) imaging scans to simultaneously quantify liver fat (using proton density fat fraction),[13] iron content (using T2* relaxation maps)[14 15] and fibroinflammation (using iron-corrected T1 relaxation maps; cT1). cT1 is an MRI metric that has been shown to correlate with composites of fibrosis and inflammation,[16–18] predict clinical outcomes[19 20] and have low interobserver variability and high repeatability over time and across scanners.[21 22] Moreover, cT1 outperformed other non-invasive techniques commonly used in the standard of care (SoC) by uniquely predicting future flares in patients with AIH who were deemed clinically 'low-risk' but had active disease on mpMR scans.[12] LiverMultiScan has also shown utility within the AIH context to significantly impact clinical decision-making and physician intended patient management plans,[23] as well as showing utility in long-term management of paediatric patients.[11]

The National Institute for Health Research (NIHR) has shown that by conducting early economic evaluation of diagnostic techniques, modelling can reduce commercial risk by providing evidence on cost-effectiveness.[24] Typically, a hypothetical early economic model is developed to compare the indicative cost consequences of using a different method versus standard testing for a particular patient group within a healthcare setting and highlight the clinical need for the proposed technology.[24] These studies help to identify the cost consequences indicating to developers the likely willingness of the payers such as the National Health Service (NHS) to adopt new technologies if these are successfully brought to market. The Lean Assessment Process (LAP) is one such method used to align evidence generation with resources available at an early stage of a healthcare device development. By establishing the feasibility (or not) of a potential technology, the LAP uses a preliminary assessment of design, value and evidence reliability.[25] Moreover, by including human factors, decision analysts and health economics experts, an understanding of stakeholder views on the potential impact of the proposed technology can be developed into a subsequent early economic evaluation.[24]

As mpMR scanning is currently not used routinely in the management of AIH patients, the aim of this study was to assess the probable cost consequences of introducing it in the care pathway. Our objective was to determine whether this novel imaging technology could be used as a robust non-invasive alternative to liver biopsy (the preferred gold standard for diagnosis and monitoring) for improving patient monitoring. The findings from this evaluation can potentially inform on possible cost savings and the feasibility of incorporating changes to the care pathway in a real-world setting and subsequent successful clinical adoption.

METHODS AND MATERIALS
Early economic evaluation to model the medium-term to longer term potential impact of using mpMR scans to monitor AIH patients was performed independently by the Oxford Academic Health Science Network as part of a study to examine the impact of mpMR scans (*LiverMultiScan*) on clinical decision-making in adult with AIH.
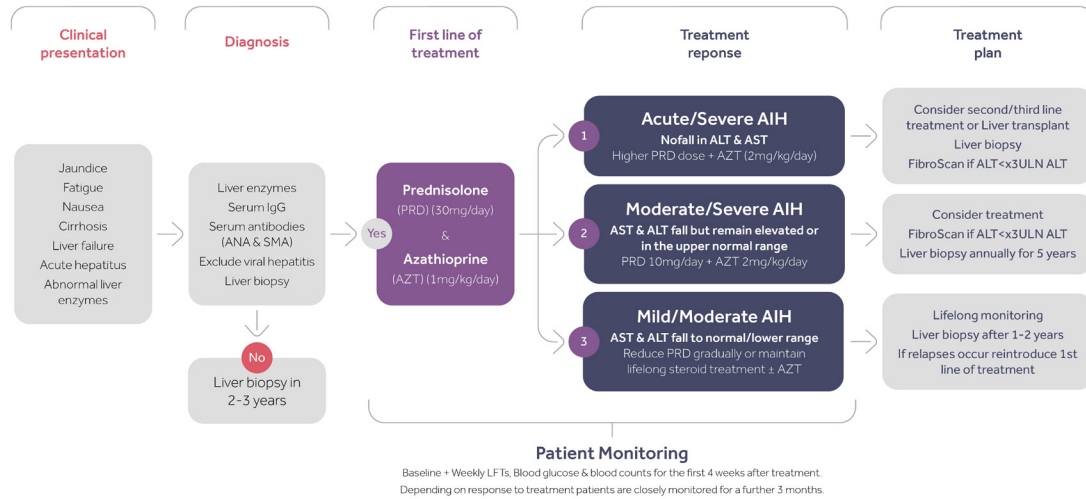
Standard care pathways
After the first line of treatment, patients with AIH follow three main routes through the SoC patient pathway, as shown in figure 1. Patients diagnosed with acute/severe AIH whose liver enzymes remain highly elevated with no change follow 'route 1' at follow-up and are either recommended for second-line/third-line treatment or a liver transplant. Patients with a good response to treatment but whose liver transaminases remain elevated or within the upper normal limit (upper-normal responders with moderate/severe AIH) follow 'route 2'. The disease progression in these patients is continuously monitored using liver transaminases, transient elastography (TE) alongside liver enzymes.[26–28] Clinical guidelines recommend that patients with suboptimal response to immunosuppression or above normal liver biochemical markers undergo a liver biopsy to better monitor subclinical disease progression.[2] Therefore, these patients are eligible to undergo an annual monitoring liver biopsy where necessary. Patients whose liver enzymes return within the normal biochemical range (normal responders with mild/moderate AIH) at follow-up are directed to 'route 3'. Typically, these patients will have lifelong monitoring using liver transaminases, TE (in the absence of inflammation) and liver biopsy every 1–2 years on average.

Modelling and resource estimates
Decision-analytic models were developed and tested to compare the indicative cost of monitoring AIH patients using the SoC versus mpMR scans (figure 1). Over a 5-year horizon, a 100 patient base case model assuming zero death or cure rates, standard monitoring recommendations and guidelines for patient care, with mpMR scans replacing liver biopsy were developed. It was assumed that mpMR scans would be used at a frequency equivalent to that quoted for biopsy, and patients would experience the associated side effects of liver biopsy at the average rates quoted in the literature.[29 30] One-way sensitivity analysis to assess the impact increasing mpMR scan frequency would have on the potential cost-savings within the overall budget for liver biopsy over the 5-year evaluation period were also investigated. Although mpMR scans can be used for postintervention monitoring in patients with severe/acute AIH, they generally require few or no additional liver biopsies postdiagnosis due to the severe persistent hepatitis. Therefore, as 'route 1' would have little impact on this early economic analysis, it was not included in the modelling. On the other hand, upper-normal (moderate/severe AIH) and normal responders (mild/moderate AIH) are more likely to undergo more histological assessment for monitoring disease progression compared with those with severe/acute AIH. Hence,

(A) Current pathway
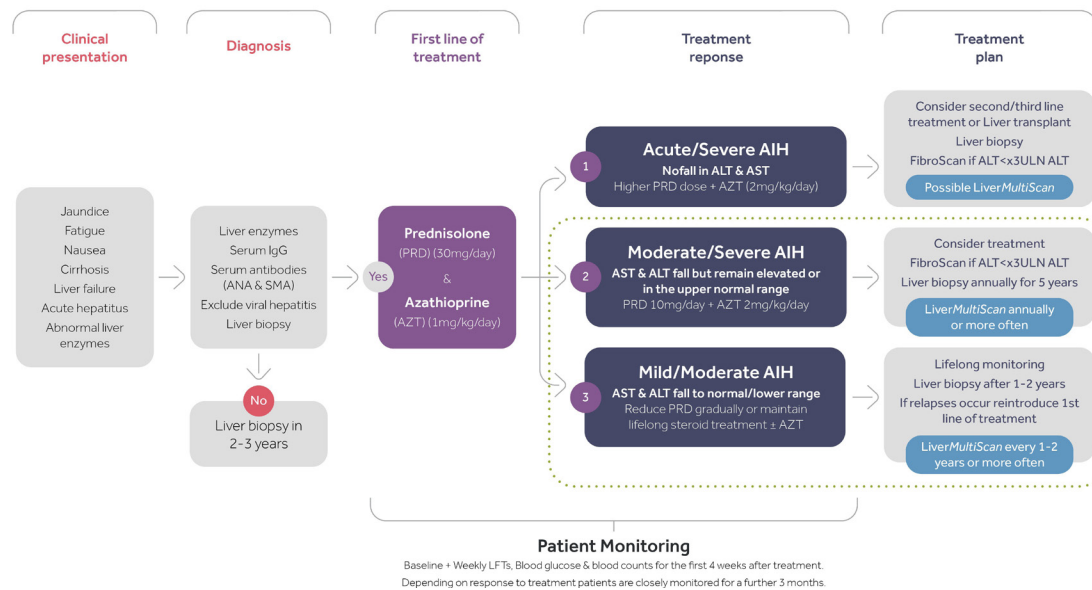

(B) Proposed pathway incorporating Liver*MultiScan*

Figure 1 Schematic diagram of the standard of care autoimmune hepatitis care pathway adapted from references.[26–28] (A) Current pathway and (B) proposed pathway incorporating *LiverMultiScan*. Route 1 is followed by patients diagnosed with severe/acute AIH; route 2 route is followed by patients diagnosed with moderate AIH and route 3 is followed by patients diagnosed with mild-to-moderate AIH. AIH, autoimmune hepatitis; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

in this work, we only considered 'route 2' and 'route 3' for modelling.

All data were collected, and modelling was performed between January and December 2019 with medical test costs obtained from the NHS 2019/2020 tariff.[31] Average biopsy-related adverse events costs and frequency of tests were included in the models as specified by the NHS and reported in the literature. The clinical pathway shown in figure 1 (including routes and assumed frequency of biopsy) was developed from clinical guidelines[26–28] and discussion with experienced hepatologists and AIH experts from St Mary's Hospital Imperial College NHS

Foundation Trust, Oxford University Hospitals NHS Foundation Trust and King's College Hospital.

Patients and public involvement
Patients and the public were not involved in the conduct of this study.

RESULTS
Base case modelling
Base case modelling to compare the costs associated with SoC using liver biopsy and the proposed pathway

Table 1 Costs of monitoring tests and health-care management assumptions used in the base case modelling.[5 29–31 36] The LiverMultiScan cost includes direct (image processing and reporting), as well as indirect and overhead costs.

Costs of monitoring tests				
Monitoring		**Tariff**		
Percutaneous punch biopsy of lesion of liver, 19 years and over		£726.00		
MRI scan of one area, without contrast, 19 years and over		£108 (plus cost of reporting £22)		
LiverMultiScan		£300.00		
Healthcare management costs of biopsy-related complications				
Possible complication	**Average cost**	**Proportion of patients**	**Additional cost of complication (per 100) per year**	**Per patient cost**
Major bleeding	£4592.50	0.5%–4.5%	£2296.25–£20666.25	
Minor bleeding	£1853.33	2.70%	£5003.99	
Abdominal pain with interventions	£2041.00	4.5%–5%	£9184.50–£10205.00	
Abdominal pain without interventions	£382.00	1%–5%	£382.00–£1910.00	
Overall average costs of complications	Upper range		£37785.24	£377.85
	Lower range		£16866.74	£168.67

using mpMR in route 2 (upper-normal responders with moderate/severe AIH) and route 3 (normal responders with mild/moderate AIH) was performed using a sample size of 100 patients per route. The cost of the monitoring tests and healthcare management costs of biopsy-related side-effects, frequencies and assumptions used in the models are summarised in table 1.

The estimated annual cost of using liver biopsy to monitor patients (SoC) (including the cost of biopsy-related adverse events) ranged between £894.67 and £1103.85 per patient; depending on the proportion of patients incurring a biopsy complication and type of complication (table 1). In comparison, the estimated annual cost of using non-contrast MRI and LiverMultiScan analysis and reporting was £430.00 (table 1). As it was assumed that all patients with moderate/severe AIH would receive an annual liver biopsy, cumulative savings ranging between £232333.70 and £336926.20 in the 100-patient cohort over 5 years (table 2), were associated with using mpMR scans at the same frequency. Furthermore, in the base case model for patients with mild/moderate AIH following route 3, it was assumed that SoC involved the use of three liver biopsies over 5 years. Subsequently, the cumulative saving savings associated with using mpMR scans compared with SoC ranged between £139400.22 and £202155.72 over 5 years (table 2).

Deterministic sensitivity analysis
One-way sensitivity analysis in patients with moderate/severe AIH showed that doubling the number of mpMR scans to 10 over 5 years (from annually to biannually), affording closer monitoring, remains cost-saving and has the potential to save between £17333.70 and £121926.20 from the overall budget for five liver biopsy and associated complications in a 100-patient cohort (table 3). Similarly, for those with mild/moderate AIH,

doubling the rate of mpMR scans from 3 to 6 over the 5-year period translated to a possible cumulative saving of between £10400.22 and £73155.72 in the 100-patient cohort over a 5-year horizon (table 3).

Minimalistic approach for all AIH patients with moderate/severe or mild/moderate AIH
Additional modelling was performed to evaluate the potential cost savings if only two liver biopsies were performed over a 5-year period in all AIH patients with either mild/moderate or moderate/severe disease in comparison to mpMR scanning. This minimalistic approach for invasive monitoring of AIH patients showed that cumulative saving associated with using mpMR scanning per 100 patients ranged between £92933.48 and £134770.48 over 5 years (table 2). Moreover, if this minimalistic approach is followed, from the overall budget for two liver biopsy and associated complications, an annual mpMR scan is associated with a potential cost-saving of up to £5770.48 in a 100-patient cohort over 5 years (table 3).

DISCUSSION
In this early economic evaluation assessing the probable cost consequences of introducing mpMR scanning into the care pathway of patients with AIH as a monitoring tool to replace liver biopsy, mpMR scanning was found to be a cost-saving alternative to liver biopsy.

Liver biopsy can be associated with high care costs particularly due to the possibility of postprocedure complications arising in approximately 32.5% of patients, which include pain (24.1%), major bleeding (3.5%), minor bleeding (2.7%), transient hypotension (1.0%) and a mortality rate of as high as 1.2%.[4 29 30] In addition in-hospital monitoring is required for all patients for at least 6–8 hours with frequent vitals and blood pressure measurements. Moreover, as up to

Table 2 Base case result for patients with moderate/severe and mild/moderate AIH.

		Costs without adverse events (£)	Annual cost of adverse events per 100 patients (£)	5-year cost of biopsy alone per 100 patients (£)	5-year cost of adverse events alone per 100 patients (£)	Total 5-year biopsy and adverse events costs per 100 patients (£)	Per patient 5-year cost (£)	Per patient annual cost (£)
Scenario: biopsy annually, over 5-year period								
Standard care (biopsy)	*Upper cost*	726.00	37785.24	363000.00	188926.20	551926.20	5519.26	1103.85
	Lower cost	726.00	16866.74	363000.00	84333.70	447333.70	4473.34	894.67
LMS and MRI		430.00				215000.00	2150.00	430.00
Total savings (liver biopsy with adverse events— LMS)	*Upper cost saving*					336926.20	3369.26	673.85
	Lower cost saving					232333.70	2323.34	464.67
Scenario: 3 biopsies, over 5-year period								
Standard care (biopsy)	*Upper cost*	726.00	37785.24	217800.00	113355.72	331155.72	3311.56	662.31
	Lower cost	726.00	16866.74	217800.00	50600.22	268400.22	2684.00	536.80
LMS and MRI	*Upper cost*	430.00	0	0	0	129000.00	1290.00	258.00
Total savings (liver biopsy with adverse events— LMS)	*Upper cost saving*					202155.72	2021.56	404.31
	Lower cost saving					139400.22	1394.00	278.80
Scenario: 2 biopsies, over 5-year period								
Standard care (biopsy)	*Upper cost*	726.00	37785.24	145200.00	75570.48	220770.48	2207.70	441.54
	Lower cost	726.00	16866.74	145200.00	33733.48	178933.48	1789.33	357.87
LMS and MRI		430.00	0	0	0	86000.00	860.00	172.00
Total savings (liver biopsy with adverse events— LMS)	*Upper cost saving*					134770.48	1347.70	269.54
	Lower cost saving					92933.48	929.33	185.87

LMS, LiverMultiScan; MRI, magnetic resonance imaging.

5% of patients may require readmission for biopsy-linked complications, including bleeding and pain, liver biopsy is an unattractive and costly way to assess for a disease flares or remission.[4 30] Percutaneous liver biopsy should only be performed when the benefits of knowing the histology outweigh the risks to the patient. In contrast to this, the proposed care pathway for monitoring AIH patients using mpMR scanning as a monitoring tool eliminates the risk of such complications, and therefore the associated costs, hospitalisation and mortality rates.

In this early economic evaluation to assess the impact of substituting liver biopsy-based monitoring with non-invasive mpMR scanning (*LiverMultiScan*) in the NHS SoC pathway for AIH patients, results show that from an economic and cost-saving perspective, mpMR scanning might have a considerable edge over liver biopsy. More specifically, the base case results from the cost analysis model indicate that the use of mpMR scanning may lead to significant cost savings of £336 926.20 for 100 upper-normal responders (moderate/severe AIH

in route 2), and £202 155.72 for 100 normal responders (mild/moderate AIH in route 2) over a 5-year horizon. More specifically, sensitivity analyses indicated that doubling the rate of monitoring for AIH patients with moderate/severe from an annual to a biannual scan and from 3 every 5 years to annually for those with mild/moderate AIH is cost saving (£121 926.20 and £73 155.72, respectively) compared with the use of liver biopsy. This is particularly important as more accurate monitoring of this cyclic relapsing disease can result in better phenotyping and patient management. These improvements may in turn improve patient outcomes which can lead to positive downstream changes in patient health. In addition to this, in the minimalistic model assuming patients receive only two liver biopsies over 5 years, replacing these two liver biopsies with annual mpMR scans over for 100 patients with AIH resulted in possible cost savings of £5770.48.

A critical determinant of cost-effectiveness in many cases evaluated by the NIHR relies on linking test results to clinical outcomes and the health consequences of

Table 3 Sensitivity analysis for costs savings in patients with moderate/severe and mild/moderate AIH.

LMS frequency over 5 years	5-year cost of biopsy per 100 patients (£) (upper cost of LMS+MRI)	5-year costs per 100 patients (£) (biopsy+adverse events)—using lower cost threshold estimate for adverse events costs	5-year cost difference per 100 patients between standard care (lower threshold of biopsy and adverse events costs) and LMS	5-year costs per 100 patients (£) (biopsy+adverse events)—using upper cost threshold estimate for adverse events costs	5-year cost difference per 100 patients between standard care (upper threshold of biopsy and adverse events costs) and LMS
Scenario: biopsy annually, over 5-year period					
5	215 000.00	447 333.70	232 333.70	551 926.20	336 926.20
6	258 000.00	447 333.70	189 333.70	551 926.20	293 926.20
7	301 000.00	447 333.70	146 333.70	551 926.20	250 926.20
8	344 000.00	447 333.70	103 333.70	551 926.20	207 926.20
9	387 000.00	447 333.70	60 333.70	551 926.20	164 926.20
10	430 000.00	447 333.70	17 333.70	551 926.20	121 926.20
11	473 000.00	447 333.70	25 666.30	551 926.20	78 926.20
12	516 000.00	447 333.70	68 666.30	551 926.20	35 926.20
Scenario: 3 biopsies, over 5-year period					
3	129 000.00	268 400.22	139 400.22	331 155.72	202 155.72
4	172 000.00	268 400.22	96 400.22	331 155.72	159 155.72
5	215 000.00	268 400.22	53 400.22	331 155.72	116 155.72
6	258 000.00	268 400.22	10 400.22	331 155.72	73 155.72
7	301 000.00	268 400.22	32 599.78	331 155.72	30 155.72
8	344 000.00	268 400.22	75 599.78	331 155.72	12 844.28
Scenario: 2 biopsies, over 5-year period					
2	86 000.00	178 933.48	92 933.48	220 770.48	134 770.48
3	129 000.00	178 933.48	49 933.48	220 770.48	91 770.48
4	172 000.00	178 933.48	6933.48	220 770.48	48 770.48
5	215 000.00	178 933.48	36 066.52	220 770.48	5770.48
6	258 000.00	178 933.48	79 066.52	220 770.48	37 229.52

LMS, LiverMultiScan; MRI, magnetic resonance imaging.

using new diagnostic tests.[24][32] Thus far, prospective studies have shown the capability of this mpMR technique to predict outcomes in patients with mixed liver disease aetiologies (including AIH),[17] in identifying underlying AIH disease activity and response to therapy,[11] in predicting future flares/relapse,[12] as well as aiding autoimmune liver disease diagnosis[11] and assessing impact on physician decision-making.[23] Therefore, there is a growing body of evidence highlighting the utility of this technique to predict adverse clinical outcomes by identifying those with active subclinical disease not identified by currently available techniques.

This study was not without its limitations. First, as reported by Dyson and colleagues,[33] there is heterogeneity in the management of AIH patients, therefore, liver biopsy may not be used as routinely by all clinicians as recommended by clinical guidelines. Therefore, some of the assumptions used in the modelling pertaining to liver biopsy frequency may not reflect the costs associated with real-world patient management. Nevertheless, in a long-term review of AIH outcomes, Gleeson[27] has shown after achievement of remission

(confirmed histologically reduced relapse rates can be achieved, however, there is still a very high relapse rate (up to 80%) if treatment is stopped after initial remission (biochemical±histological). Consequently, to compensate for this, a minimalistic model considering replacing two biopsies over 5 years with mpMR scanning was investigated. Although clinical guidelines have been updated more recently to reflect the changes in the use of liver biopsy,[34] it is still recognised as the gold standard for diagnosis and disease monitoring. The need for non-invasive technologies to replace liver biopsy is becoming more widely recognised.[35] Second, although a small number of patients with AIH reach complete remission, during the base case modelling we assumed zero cure rates. This assumption was made as the data required for such analyses, including the healthcare costs associated with AIH patient management, can only be obtained from real-world evaluations implementing the suggested hypothetical model. Therefore, as the early economic evaluation suggests that using mpMR scanning for monitoring in AIH is cost-saving, future work should investigate the feasibility of implementing this hypothetical monitoring model across

different trusts in the NHS. This model would also need to account for discount costs depending on the most appropriate payment mode accepted by the NHS payors. Moreover, additional testing could improve overall patient care, which may have other direct and indirect health service cost savings. Thus, as non-invasive techniques can significantly improve patient monitoring, we recommend that a full economic evaluation be performed using trial and real-world data—incorporating analyses evaluating quality-adjusted life year gains into the cost model—to fully quantify the improvement in healthcare the inclusion of mpMR scanning in the SoC might bring.

Overall, our analysis suggests that the integration of non-invasive mpMR scanning in AIH patient pathways has the potential to improve the monitoring care pathway and may result in cost savings for AIH patients in secondary care in the NHS in England. Moreover, more frequent, and detailed phenotyping could lead to improvements in patient outcomes, such as better titrated immunosuppression for individual patients. With more research data, from clinical trial and real-world usage monitoring, a more in-depth economic evaluation of the impact on the adoption of mpMRI into the AIH patient monitoring pathway can be produced.

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REFERENCES

1 Webb GJ, Ryan RP, Marshall TP, *et al*. The epidemiology of UK autoimmune liver disease varies with geographic latitude. *Clin Gastroenterol Hepatol* 2021;19:2587–96.

2 European Association for the Study of the Liver. EASL clinical practice guidelines: autoimmune hepatitis. *J Hepatol* 2015;63:971–1004.

3 Terziroli Beretta-Piccoli B, Mieli-Vergani G, Vergani D. Autoimmune hepatitis: standard treatment and systematic review of alternative treatments. *World J Gastroenterol* 2017;23:6030–48.

4 Thomaides-Brears HB, Alkhouri N, Allende D, *et al*. Incidence of complications from percutaneous biopsy in chronic liver disease: a systematic review and meta-analysis. *Dig Dis Sci* 2022;67:3366-3394.

5 Myers RP, Fong A, Shaheen AAM. Utilization rates, complications and costs of percutaneous liver biopsy: a population-based study including 4275 biopsies. *Liver Int* 2008;28:705–12.

6 Kalambokis G, Manousou P, Vibhakorn S, *et al*. Transjugular liver biopsy--indications, adequacy, quality of specimens, and complications--a systematic review. *J Hepatol* 2007;47:284–94.

7 Bedossa P, Carrat F. Liver biopsy: the best, not the gold standard. *J Hepatol* 2009;50:1–3.

8 Mahmud N, Doshi SD, Forde KA, *et al*. Transient elastography reliably estimates liver fibrosis in autoimmune hepatitis. *Clin Exp Hepatol* 2019;5:244–9.

9 Dhaliwal HK, Hoeroldt BS, Dube AK, *et al*. Long-Term prognostic significance of persisting histological activity despite biochemical remission in autoimmune hepatitis. *Am J Gastroenterol* 2015;110:993–9.

10 Gordon V, Adhikary R, Appleby V, *et al*. Diagnosis, presentation and initial severity of autoimmune hepatitis (AIH) in patients attending 28 hospitals in the UK. *Liver Int* 2018;38:1686–95.

11 Janowski K, Shumbayawonda E, Cheng L, *et al*. Quantitative multiparametric MRI as a non-invasive stratification tool in children and adolescents with autoimmune liver disease. *Sci Rep* 2021;11:15261.

12 Arndtz K, Shumbayawonda E, Hodson J, *et al*. Multiparametric magnetic resonance imaging, autoimmune hepatitis, and prediction of disease activity. *Hepatol Commun* 2021;5:1009–20.

13 Wilman HR, Kelly M, Garratt S, *et al*. Correction: characterisation of liver fat in the UK Biobank cohort. *PLoS One* 2017;12:e0176867.

14 McKay A, Wilman HR, Dennis A, *et al*. Measurement of liver iron by magnetic resonance imaging in the UK Biobank population. *PLoS One* 2018;13:e0209340.

15 Mozes FE, Tunnicliffe EM, Moolla A, *et al*. Mapping tissue water T_1 in the liver using the MOLLI T_1 method in the presence of fat, iron and B_0 inhomogeneity. *NMR Biomed* 2019;32:e4030.

16 Eddowes PJ, McDonald N, Davies N, *et al*. Utility and cost evaluation of multiparametric magnetic resonance imaging for the assessment of non-alcoholic fatty liver disease. *Aliment Pharmacol Ther* 2018;47:631–44.

17 Pavlides M, Banerjee R, Tunnicliffe EM, *et al*. Multiparametric magnetic resonance imaging for the assessment of non-alcoholic fatty liver disease severity. *Liver Int* 2017;37:1065–73.

18 McDonald N, Eddowes PJ, Hodson J, *et al*. Multiparametric magnetic resonance imaging for quantitation of liver disease: a two-centre cross-sectional observational study. *Sci Rep* 2018;8:9189.

19 Rider OJ, Banerjee R, Rayner JJ, *et al*. Investigating a liver fat: arterial stiffening pathway in adult and childhood obesity. *Arterioscler Thromb Vasc Biol* 2016;36:198–203.

20 Pavlides M, Banerjee R, Sellwood J, *et al*. Multiparametric magnetic resonance imaging predicts clinical outcomes in patients with chronic liver disease. *J Hepatol* 2016;64:308–15.

21 Bachtiar V, Kelly MD, Wilman HR, *et al*. Repeatability and reproducibility of multiparametric magnetic resonance imaging of the liver. *PLoS One* 2019;14:e0214921.

22 Harrison SA, Dennis A, Fiore MM, *et al*. Utility and variability of three non-invasive liver fibrosis imaging modalities to evaluate efficacy of GR-MD-02 in subjects with NASH and bridging fibrosis during a phase-2 randomized clinical trial. *PLoS One* 2018;13:e0203054.

23 Heneghan MA, Shumbayawonda E, Dennis A, *et al*. Quantitative magnetic resonance imaging to aid clinical decision making in autoimmune hepatitis. *EClinicalMedicine* 2022;46:101325.

24 Abel L, Shinkins B, Smith A, *et al*. Early economic evaluation of diagnostic technologies: experiences of the NIHR diagnostic evidence Co-operatives. *Med Decis Making* 2019;39:857–66.

25 Ni M, Borsci S, Bajre M. The Lean Assessment Process (LAP) – experiences of NIHR London IVD Cooperative working with early stage medical technologies. Prague, Czech Republic, World Congress on Medical Physics & Biomedical Engineering, IUPEM 2017.

26 Manns MP, Czaja AJ, Gorham JD, *et al*. Diagnosis and management of autoimmune hepatitis. *Hepatology* 2010;51:2193–213.

27 Gleeson D, Heneghan MA, British Society of Gastroenterology. British Society of gastroenterology (Bsg) guidelines for management of autoimmune hepatitis. *Gut* 2011;60:1611–29.

28 Makol A, Watt KD, Chowdhary VR. Autoimmune hepatitis: a review of current diagnosis and treatment. *Hepat Res Treat* 2011;2011:1–11.

29 Seeff LB, Everson GT, Morgan TR, *et al*. Complication rate of percutaneous liver biopsies among persons with advanced chronic liver disease in the HALT-C trial. *Clin Gastroenterol Hepatol* 2010;8:877–83.

30 Al-Ghamdi A. Complications of Liver Biopsy. In: Takahashi H, ed. *Liver biopsy*. Rijeka, Croatia: InTech, 2011: 363–70.

31 National Health Service (NHS), 2019/2020. 2019/20 National Tariff Payment System: national prices and prices for emergency care services. [Online]. Available: https://www.england.nhs.uk/publication/past-national-tariffs-documents-and-policies/

32 Ferrante di Ruffano L, Hyde CJ, McCaffery KJ, *et al*. Assessing the value of diagnostic tests: a framework for designing and evaluating trials. *BMJ* 2012;344:e686.

33 Dyson JK, Wong LL, Bigirumurame T, *et al*. Inequity of care provision and outcome disparity in autoimmune hepatitis in the United Kingdom. *Aliment Pharmacol Ther* 2018;48:951–60.

34 Mack CL, Adams D, Assis DN, *et al*. Diagnosis and management of autoimmune hepatitis in adults and children: 2019 practice guidance and guidelines from the American association for the study of liver diseases. *Hepatology* 2020;72:671–722.

35 European Association for the Study of the Liver. Electronic address: easloffice@easloffice.eu, Clinical Practice Guideline Panel, Chair:, *et al*. EASL Clinical Practice Guidelines on non-invasive tests for evaluation of liver disease severity and prognosis - 2021 update. *J Hepatol* 2021;75:659–89.

36 Thampanitchawong P, Piratvisuth T. Liver biopsy:complications and risk factors. *World J Gastroenterol* 1999;5:301–4.