EE209

Non-invasive tests (NITs) to risk-stratify patients with noncirrhotic metabolic-associated steatohepatitis (MASH) in a specialty setting who are eligible for resmetirom: cost-effectiveness analysis from a US payer perspective

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INTRODUCTION

- Resmetirom was conditionally FDA approved in March 2024 for adults with noncirrhotic MASH with moderate to advanced fibrosis (consistent with F2 and F3 liver fibrosis).
- While liver biopsy (LB) has been the reference standard for diagnosis and staging, its invasiveness, high cost, sampling variability and risk underscore the need for NITs to identify patients who would be eligible for resmetirom in the U.S.
- Accurate diagnosis of patients with moderate to advanced (F2–F3) noncirrhotic MASH, who are eligible for treatment with resmetirom, is essential for optimizing clinical decision-making and access to care.[1]
- This study assessed the cost-effectiveness (CE) of different NIT strategies for identifying resmetirom-eligible patients with MASH-related fibrosis compared to a combination of NITs + LB for discordant cases. This analysis evaluates multiple NIT sequences using a variety of tests, reflecting clinical practice in specialty care.

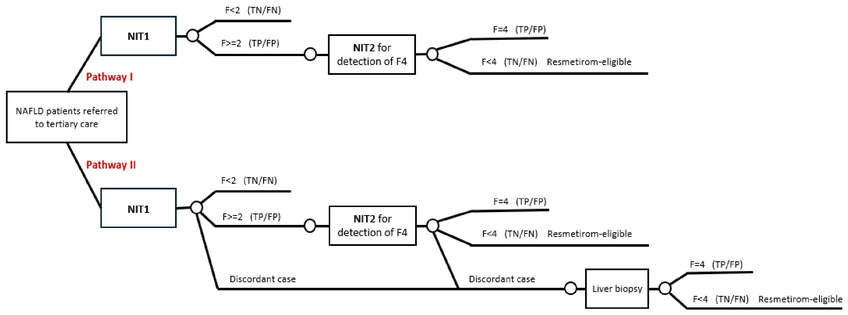
METHODS

- A cost-utility model was developed, combining a decision tree and Markov model, to reflect the variability in diagnostic testing strategies and the complexities of managing liver disease progression, with and without treatment with resmetirom.
- The model simulated patients referred to specialty care in the U.S. for suspected non-alcoholic fatty liver disease, with or without fibrosis.
- The decision-tree model (Figure 1) simulated various testing pathways using two-step NIT sequences, defined by pre-specified cut-off thresholds (Table 1):
  1. The first NIT (NIT1) identified significant to advanced MASH fibrosis (F≥2).
  2. The second NIT (NIT2) ruled out cirrhosis (F4).
- In the comparator arm (Pathway II), a LB was included in cases where NIT1 or NIT2 results were discordant. The model assumes that 5% of cases undergo LB.
- Three categories of NITs were assessed: blood-based, imaging-based, and combined modalities.
- Those diagnosed with moderate to advanced fibrosis (F2–F3) were considered eligible for resmetirom treatment.
- Upon diagnosis, patients transitioned into the Markov model to evaluate the long-term CE of resmetirom treatment compared with placebo over a lifetime horizon, using a willingness-to-pay (WTP) threshold of $100,000 per quality-adjusted life-year. This component of the model was adapted from Javanbakht et al., 2023.[2]

Table 1. Cut-off thresholds of included NITs

Category	NIT1 to identify F≥2 fibrosis	NIT2 to identify F4 fibrosis
Blood-based	• FIB4 > 0.8 • ELF ≥ 8.8 • MASEF ≥ 0.33 • NIS2+ ≥ 0.4564 • NIS2+ ≥ 0.6815 • NIS4 ≥ 0.539 • FibroTest ≥ 0.35	• FIB4 ≥ 3.48 • NIS4 ≥ 0.9 • FibroTest >= 0.74 • ELF ≥ 10.9 • ELF ≥ 11.3
Imaging-based	• VCTE ≥ 8 kPa • Liver MultiScan cT1 ≥ 875 ms • FAST ≥ 0.67	• VCTE ≥ 20.9 kPa • MRE ≥ 4.7 kPa

Figure 1. Decision tree model structure



RESULTS

- Using 10 potential tests for NIT1 and 7 for NIT2, the analysis resulted in 55 uniquely possible NIT combinations (Figure 2).
- The resulting combinations were ranked based on accuracy and QALY gains from lifelong treatment.
- All imaging-based NIT sequences were found cost-effective at the WTP threshold of $100,000 per QALY gained when LB was not part of the diagnostic pathway.
- The CE of the most accurate NIT combinations in each category are presented in Table 2.
- Among these strategies, the imaging-based combination using VCTE ≥ 8kPa and MRE ≥ 4.7kPa demonstrated the highest net monetary benefit of $2,358, making it the most cost-effective approach, compared with the same respective sequence followed by LB for discordant cases.

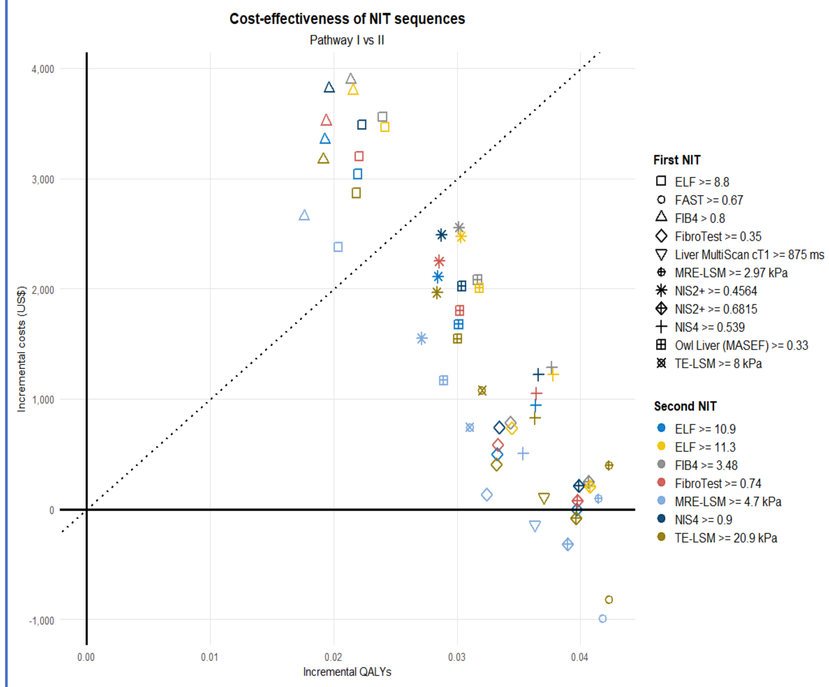
LIMITATIONS

- This CE study does not account for any diagnostic testing that may have occurred in primary care or prior to specialty care referral, and it does not capture potential re-evaluations or changes in disease progression over time.

Table 2. Cost-effectiveness of most accurate NIT sequences

Category	NIT1	NIT2	Incremental costs per patient	Incremental QALYs per patient	ICER	NMB
Blood-based	ELF ≥ 8.8	ELF ≥ 11.3	$3,466	0.024	$143,380	-$1,049
Blood-imaging	ELF ≥ 8.8	MRE ≥ 4.7 kPa	$2,377	0.020	$116,525	-$337
Imaging-based	VCTE ≥ 8 kPa	MRE ≥ 4.7 kPa	$745	0.031	$24,002	$2,358

Figure 2. Cost-effectiveness of various NIT sequences



CONCLUSIONS

- A NIT-only strategy reduces reliance invasive and costly LBs and can improve patient access to resmetirom treatment while maintaining cost efficiency in a specialty setting.
- Imaging-based NITs offer the most cost-effective approach for diagnosing moderate to advanced (F2–F3) noncirrhotic MASH, while enhancing diagnostic efficiency. TE and MRE in particular, have shown promise in accurately diagnosing liver fibrosis and have strong potential for future advancements that could further improve diagnostic accuracy and differentiation of liver conditions.
- These findings highlight the value of integrating NIT-only strategies to enhance patient access to emerging therapies, support payer value, and optimize healthcare resources.
- This study demonstrated that wider adoption of NIT-only strategies, particularly focusing on imaging tests, can be cost effective and improve long-term patient outcomes.

REFERENCES

1. Noureddin et al. Clin Gastroenterol Hepatol. 2024 Dec;22(12):2367-2377.
2. Javanbakht et al. PharmacoEconomics – open 2023, 7(1), 93–110.

ABBREVIATIONS

CE, cost-effectiveness; ELF, enhanced liver fibrosis; FIB4, fibrosis-4 index; ICER, incremental cost-effectiveness ratio; LB, liver biopsy; MASH, metabolic-associated steatohepatitis; MRE, magnetic resonance elastography; NIT, Non-invasive tests; NMB, net monetary benefit; QALYs, quality-adjusted life-years; VCTE, vibration-controlled transient elastography.

DISCLOSURES

- Madrigal Pharmaceuticals Inc. provided the funding for this research, which was conducted by Optimax Access.
- This economic analysis is focused on the U.S. and accordingly uses U.S. costs and pricing