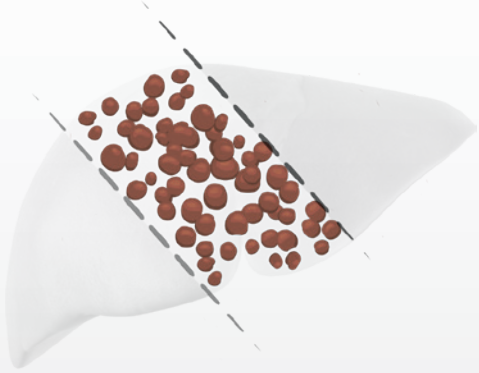

MASLD Screening Strategies

Cost-effectiveness of Sequential Strategies Using Non-invasive Tests (NITs)

Identifying Liver Fibrosis and Risk Stratifying MASLD Patients in Primary Care

Introduction

Metabolic dysfunction-associated steatotic liver disease (MASLD) represents a major health burden, with a global prevalence of about 30 percent.[1] Despite its prevalence, MASLD is a silent and largely undiagnosed condition[2] and fibrosis is a key factor driving the progression to adverse clinical outcomes,[3] including liver failure and hepatocellular carcinoma. Recent clinical practice guidelines (CPGs) from several major international societies[4-7] recommend using non-invasive tests (NITs) for liver fibrosis to risk-stratify MASLD patients in primary care and non-hepatology settings and to identify those at risk for adverse outcomes early. Demonstrating the cost-effectiveness of these strategies can accelerate their adoption and implementation into routine clinical practice by policymakers and healthcare providers. Recent economic studies suggest using such sequential strategies with NITs are cost-effective compared to standard of care (SoC) in the U.S. and U.K.

To evaluate the cost-effectiveness of screening strategies for high-risk MASLD in primary care in the United States, Z. Younossi et al.[8] referred to the diagnostic pathways recommended by recent international, clinical-practice guidelines and used three NITs—the fibrosis-4 index (FIB-4), Enhanced Liver Fibrosis (ELF), and vibration-controlled transient elastography (VCTE). See Figure 1 for more details.

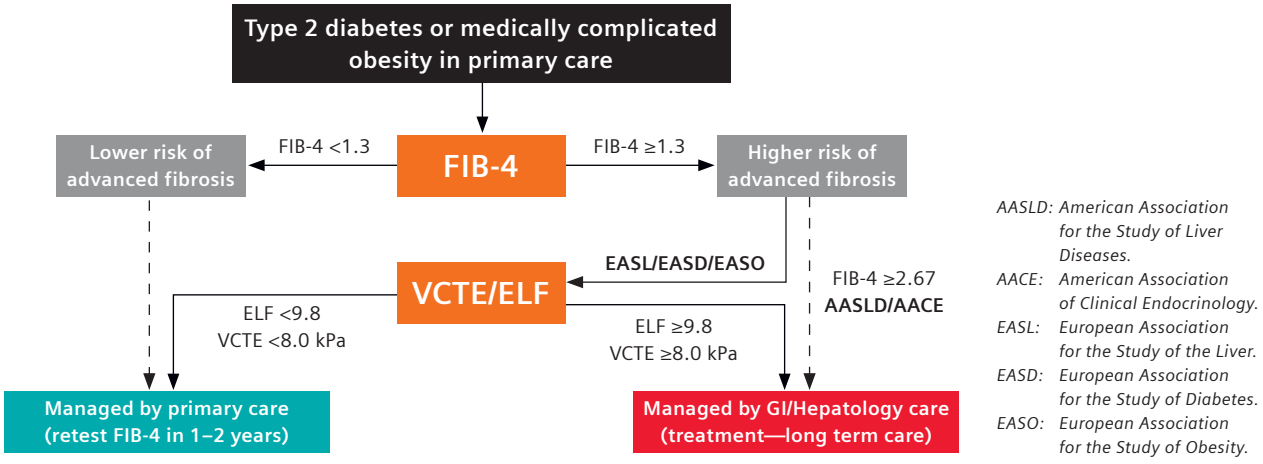

Figure 1. Overview of the pathways to screen for high-risk MASLD patients in primary care with references to recommendations from AASLD, AACE, and EASL/EASD/EASO.

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The authors developed a cost-utility analysis structured (Figure 2) with an initial decision tree capturing the diagnostic accuracy of each screening strategy based on the diagnostic accuracy of the NITs.[9,10] This was followed by a Markov model for long-term outcomes. The model focused on two high-risk groups of patients, type 2 diabetes (T2D) and medically complicated obese patients (MCO), following CPG recommendations to not screen the general population for MASLD due to the high rates of unnecessary tests.

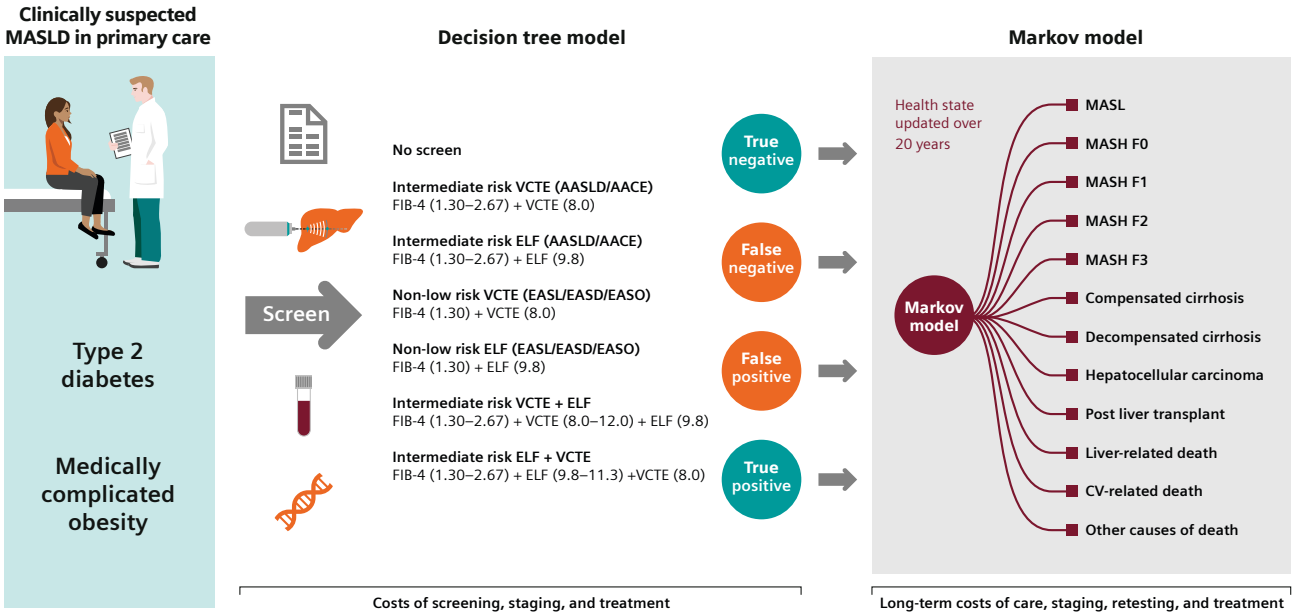

Figure 2. Structure of the model adapted from *Pharmaco-Economic Assessment of Screening Strategies for High-Risk MASLD in Primary Care*.[8]

This study suggests that screening T2D and MCO patients with NITs is cost-effective versus no screening in primary-care settings in the U.S. Although the screening strategies increased overall costs per patient, they also resulted in lower costs of long-term care compared to no screening due to reduced long-term complications and mortality.

As VCTE may not be widely available in primary-care settings in the U.S., the authors evaluated the cost-effectiveness of the screening strategies with NITs in different scenarios (Scenario 1: VCTE available in 20 percent of primary care and Scenario 2: VCTE is unavailable in primary-care settings). The outcomes of their analysis showed that "the cost-effectiveness of the MASLD screening strategies was generally consistent across the scenarios considered" when using ELF instead of VCTE. ELF therefore offers a practical and cost-effective alternative to VCTE in primary care.

The quality-adjusted life years (QALYs) for the six screening strategies ranged from 6.5259 to 6.5475 for T2D patients and from 9.0928 to 9.1032 for MCO patients—a gain over the QALY outcomes without screening, which were 6.0185 for T2D patients and 8.4766 for MCO patients.

The resulting incremental cost-effectiveness ratios (ICERs) ranged from $26,913 to $27,884 per QALY for T2D patients and from $23,265 to $24,992 per QALY for MCO patients. These ICERs are well below the U.S. willingness-to-pay threshold of $50,000 per QALY,[11] highlighting that these strategies for high-risk MASLD groups would be considered cost-effective by U.S. payers.

In a second analysis, Z. Younossi et al. recently investigated whether testing strategies with the same three NITs (FIB-4, ELF or VCTE) would also be cost-effective in the U.K.[12] (Figure 3). These strategies were compared to the current standard of care (SoC) which includes three consultations with a primary-care physician, three routine blood tests, and one ultrasound.

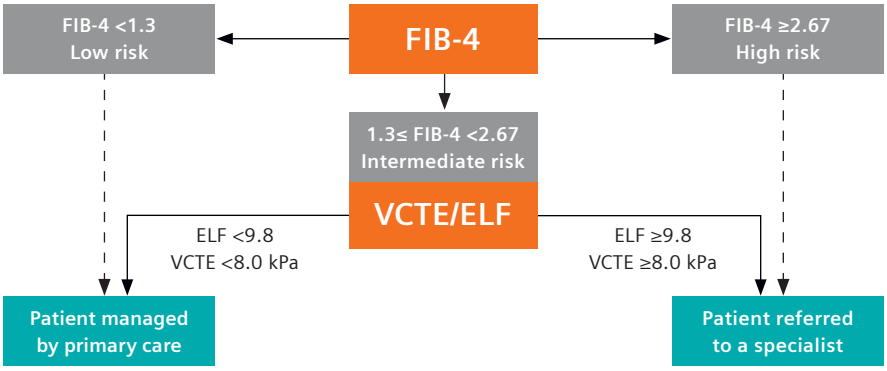

Figure 3. Sequential testing pathways with NITs (FIB-4 followed by ELF or VCTE) for identifying high-risk MASLD.

The economic evaluation of the pathways was performed with a modeled cohort of MASLD patients with a relatively low prevalence of advanced fibrosis (estimated at 4.20 percent) as typically seen in U.K. primary care.[13] The model structure is similar to the one used for the US analysis with a decision tree followed by a Markov model as represented in Figure 4.

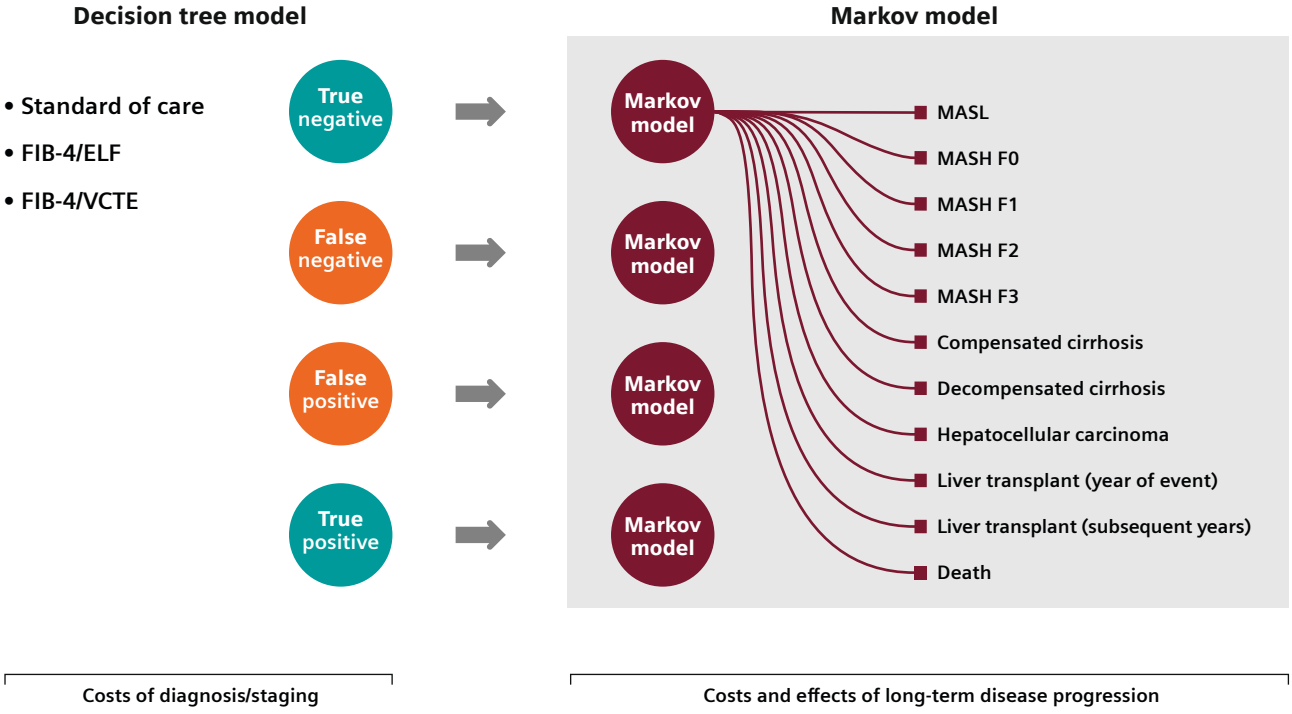

Figure 4. Model structure adapted from *Economic Evaluation of Non-invasive Test Pathways for High-risk Metabolic Dysfunction-associated Steatotic Liver Disease (MASLD) in the United Kingdom (UK).*[12]

Cost outcomes of the analysis are presented in British pounds (GBP) in Table 1. While the strategies using NIT pathways would entail higher initial diagnostic costs, they result in overall savings versus SoC. This results from lower staging costs versus SoC, driven by a significant reduction in unnecessary referrals to liver specialists: -33.71 percent for FIB-4/ELF and -40.57 percent for FIB-4/VCTE. False positive referrals represented 80 percent of the staging costs for SoC compared to 63 to 66 percent for the sequential diagnostic pathways. Unlike the assessment conducted for the United States,[8] QALYs would be unaffected by the choice of pathway in this study likely due to the shorter three-year timeframe (compared to 20 years), the low prevalence of advanced fibrosis in the modeled population and the lack of approved pharmaceutical therapies for MASLD in the UK.

Table 1. Total costs for each strategy in the UK.

Costs per patient (GBP)	Diagnostic cost (GBP)	Staging cost (GBP)	Long-term cost (GBP)	Total cost (GBP)	QALY
Standard of care	0.00	180.42	833.72	**1014.15**	2.1793
FIB-4 / ELF	15.21	145.17	832.76	**993.15**	2.1793
FIB-4 / VCTE	18.95	131.65	832.77	**983.37**	2.1793

Finally, the authors emphasized that while both NIT pathways using FIB-4, ELF, and VCTE are cost-effective compared to SoC, use of VCTE in primary care is often limited by availability constraints and the need for specialized training. In contrast, ELF testing can be easily ordered through standard laboratory facilities, making it more practical for primary care environments. However, the authors note that cost of ELF can also vary in different settings.[14]

The economic value of NITs (i.e. FIB-4, ELF, VCTE) in the U.K. had previously been examined in a pioneering article by Srivastava et al. in 2019.[15] In this study, the authors used a probabilistic decision model to assess the clinical performance and cost-effectiveness of different testing strategies using NITs for detecting advanced liver fibrosis in nonalcoholic fatty liver disease (NAFLD) patients in the context of a primary care setting in the U.K. (Author's note: The term MASLD is now used to replace NAFLD since 2023[16]). Four testing strategies were selected:

1. FIB-4 followed by ELF for patients with intermediate FIB-4 results (FIB-4/ELF)
2. FIB-4 followed by VCTE for intermediate FIB-4 (FIB-4/VCTE)
3. ELF alone*
4. VCTE alone

These strategies were compared to standard of care (SoC), which was clinical history, patient's examination, blood liver fibrosis tests, and liver ultrasound.

Like the study by Z. Younossi,[12] the authors showed that implementing NITs would significantly reduce unnecessary referrals of patients with mild disease, thereby optimizing resource utilization compared to SoC. Figure 5 illustrates that the most significant reduction in referrals—85 percent compared to SoC—was achieved through a sequential testing strategy that combined FIB-4 as the first-line test followed by ELF for patients with intermediate FIB-4 results.

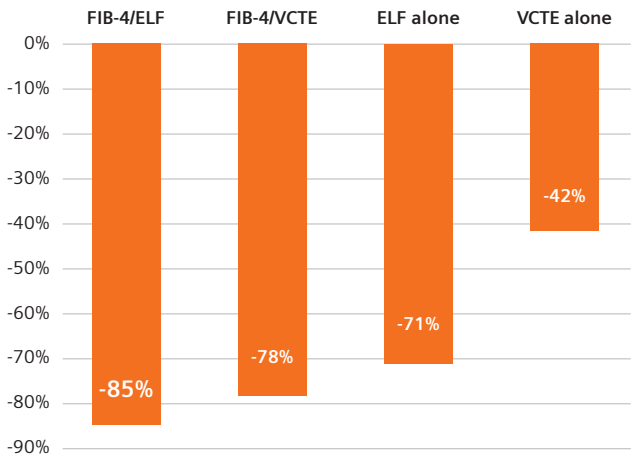

Figure 5. Change in hospital referrals driven by each NIT strategy vs. SoC.

*Note from the editor: ELF is not a standalone test, as it is indicated for use in conjunction with other laboratory findings and clinical assessments to provide a comprehensive evaluation of liver fibrosis.

In conclusion, despite methodological differences and assessments conducted in various healthcare systems, the studies presented here confirm that testing strategies using NITs for liver fibrosis are cost-effective and can significantly reduce healthcare costs in managing MASLD. One of the major benefits of NIT pathways is their ability to decrease unnecessary referrals to gastroenterology / liver clinics, which are already facing a shortage of specialists and are overburdened.[17] These positive economic outcomes can support increased awareness among primary-care physicians and healthcare payers and ultimately facilitate patient access for upcoming or already approved MASH therapies.

More about ELF

- ELF is a blood test that uses three direct markers of liver fibrosis: hyaluronic acid (HA), amino-terminal propeptide of type III procollagen (PIIINP), and tissue inhibitor of matrix metalloproteinase 1 (TIMP-1). The utility of ELF is demonstrated for the assessment of the severity of liver fibrosis in patients with chronic liver disease.[8,9]
- Outside the United States, ELF is CE-marked for the assessment of liver fibrosis severity in patients with signs, symptoms, or risk factors of chronic liver disease to support diagnosis of fibrosis staging or prognosis for likelihood of progression to cirrhosis and liver-related clinical events.

Talk to your Siemens Healthineers representative to learn more about ELF testing and don't miss the opportunity to demonstrate the vital role and value of your clinical laboratory in MASLD patient management. Also discover the complete menu of solutions and tests that our company offers to manage chronic liver diseases.

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Siemens Healthineers AG
Siemensstr. 3
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