Chronic liver disease in Europe

Diagnostic innovation and models of care to improve fibrosis detection and risk stratification in steatotic liver disease

Nicola Pugliese,[a,b,an] Trenton M. White,[c,d,an] Paul N. Brennan,[e,an] Silvana Pannain,[f] Hannes Hagström,[g,h,1] Maurice Michel,[i,j] Lisa Rice-Duek,[c] Giovanni Targher,[k,l] Cyrielle Caussy,[m] John F. Dillon,[n] Frank Tacke,[o] Christopher J. Kopka,[c] Giada Sebastiani,[p] Jerome Boursier,[q,r] Emmanuel A. Tsochatzis,[s] Willem Pieter Brouwer,[t] Giovanni Guaraldi,[u] Roberto Vettor,[a,v] Maja Thiele,[w,x] Michael Roden,[y,z,aa] Norbert Stefan,[ab,ac] Helen Jarvis,[ad] Pere Gines,[ae] Jörn M. Schattenberg,[i,j] Elisa Pose,[ae,af,ag] Stefan Buttigieg,[ah,ai] Christopher D. Byrne,[aj,ak,ao] and Jeffrey V. Lazarus[c,d,al,am,*,ao]

[a]Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Milan, Italy
[b]Division of Internal Medicine and Hepatology, Department of Gastroenterology, IRCCS Humanitas Research Hospital, Rozzano, Milan, Italy
[c]Barcelona Institute for Global Health (ISGlobal), Barcelona, Spain
[d]City University of New York Graduate School of Public Health and Health Policy (CUNY SPH), New York, NY, USA
[e]Division of Molecular and Clinical Medicine, University of Dundee, Dundee, Scotland, United Kingdom
[f]Section of Endocrinology, Diabetes and Metabolism, University of Chicago Medicine, Chicago, IL, USA
[g]Division of Hepatology, Department of Upper GI, Karolinska University Hospital, Stockholm, Sweden
[h]Department of Medicine, Huddinge, Karolinska Institutet, Stockholm, Sweden
[i]Department of Internal Medicine II, University Medical Centre Saarland, Homburg, Germany
[j]Faculty of Medicine, Saarland University, Saarbrücken, Germany
[k]Metabolic Diseases Research Unit, IRCCS Sacro Cuore - Don Calabria Hospital, Verona, Italy
[l]Department of Medicine, University of Verona, Verona, Italy
[m]Département Endocrinologie, Diabète et Nutrition, Hôpital Lyon Sud, Hospices Civils de Lyon, Pierre-Bénite, Lyon, France
[n]School of Medicine, University of Dundee, Dundee, United Kingdom
[o]Department of Hepatology and Gastroenterology, Charité - Universitätsmedizin Berlin, Campus Virchow-Klinikum and Campus Charité Mitte, Berlin, Germany
[p]Division of Gastroenterology and Hepatology, McGill University Health Centre, Montreal, Quebec, Canada
[q]Université d'Angers, HIFIH, SFR ICAT, Angers, France
[r]Department of Hepatogastroenterology, CHU Angers, Angers, France
[s]UCL Institute for Liver and Digestive Health, Royal Free Hospital and UCL, London, United Kingdom
[t]Department of Gastroenterology and Hepatology, Erasmus MC University Medical Center, Rotterdam, the Netherlands
[u]Modena HIV Metabolic Clinic, University of Modena and Reggio Emilia, Modena, Italy
[v]Center for Metabolic and Nutrition Related Diseases, IRCCS Humanitas Research Hospital, Rozzano, Milan, Italy
[w]Centre for Liver Research, Department of Gastroenterology and Hepatology, Odense University Hospital, Odense, Denmark
[x]Institute of Clinical Research, University of Southern Denmark, Odense, Denmark
[y]Department of Endocrinology and Diabetology, Medical Faculty and University Hospital Düsseldorf, Heinrich Heine University Düsseldorf, Düsseldorf, Germany
[z]Institute for Clinical Diabetology, German Diabetes Center (DDZ), Leibniz Center for Diabetes Research at Heinrich Heine University Düsseldorf, Düsseldorf, Germany
[aa]German Center for Diabetes Research (DZD), München-Neuherberg, Germany

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Abbreviations: AI, Artificial intelligence; ALD, Alcohol-associated liver disease; BMI, Body mass index; CVD, Cardiovascular disease; EHR, Electronic health record; ELF, Enhanced Liver Fibrosis; EU, European Union; FIB-4, Fibrosis-4 index; HCC, Hepatocellular carcinoma; HCP, Healthcare professional; MASH, Metabolic dysfunction-associated steatohepatitis; MASLD, Metabolic dysfunction-associated steatotic liver disease; MetALD, Metabolic dysfunction- and alcohol-associated liver disease; MetS, Metabolic syndrome; ML, Machine learning; MoC, Model of care; MRI, Magnetic resonance imaging; MRE, Magnetic resonance elastography; NCD, Non-communicable disease; NIT, Non-invasive test; PCP, Primary care provider; PoC, Point-of-care; PRS, Polygenic risk score; SLD, Steatotic liver disease; T2D, Type 2 diabetes; VCTE, Vibration-controlled transient elastography

*Corresponding author. Barcelona Institute for Global Health (ISGlobal), Barcelona, Spain.
E-mail address: jeffrey.lazarus@isglobal.org (J.V. Lazarus).

[an]These authors share first authorship.
[ao]These authors share senior authorship.
[1]Deceased.

[ab]Department of Internal Medicine IV, Division of Endocrinology, Diabetology, and Nephrology, University of Tübingen, Tübingen, Germany
[ac]Institute of Diabetes Research and Metabolic Diseases, Helmholtz Center Munich, Tübingen, Germany
[ad]Population and Health Sciences Institute, Newcastle University, Newcastle upon Tyne, United Kingdom
[ae]Liver Unit, Hospital Clínic of Barcelona, Barcelona, Spain
[af]Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain
[ag]Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBEREHD), Madrid, Spain
[ah]Digital Public Health Task Force, Association of Schools of Public Health in the European Region (ASPHER), Brussels, Belgium
[ai]Ministry for Health and Active Ageing, Valletta, Malta
[aj]School of Human Development and Health, Faculty of Medicine, University of Southampton, Southampton, United Kingdom
[ak]National Institute for Health and Care Research Southampton Biomedical Research Centre, University of Southampton and University Hospital Southampton National Health Service Foundation Trust, Southampton, United Kingdom
[al]Faculty of Medicine and Health Sciences, University of Barcelona (UB), Barcelona, Spain
[am]Chair, *The Lancet Regional Health – Europe* Series on chronic liver disease in Europe

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Summary

Steatotic liver disease (SLD) is the leading cause of chronic liver disease in Europe, with liver fibrosis representing the strongest predictor of liver-related outcomes and an important contributor to cardiometabolic risk. This Series paper examines diagnostic innovation and models of care to improve fibrosis detection and risk stratification across the continuum of care for SLD. A growing range of non-invasive tests for fibrosis assessment is now available, including blood-based biomarkers, imaging modalities, automated laboratory algorithms, and artificial intelligence-enabled tools. However, implementation remains inconsistent because of limited awareness, restricted geographic and financial access to advanced diagnostics, fragmented referral pathways, heterogeneous reimbursement, limited use of automated reflex testing, and poor digital integration across laboratories and electronic health records. Integrated multidisciplinary models of care linking primary care with specialist services may improve early fibrosis detection, referral efficiency, and equitable access to risk-stratified management, particularly among people living with indicator conditions such as type 2 diabetes and obesity.

Keywords: MASLD; metALD; Non-invasive tests; Diagnostic innovation; Fibrosis detection; Risk stratification; Models of care; Blood-based biomarkers; Diagnostic pathways; Precision hepatology

Introduction

In 2023, an international consensus redefined the nomenclature and taxonomy of fatty liver diseases under the umbrella term steatotic liver disease (SLD), marking a shift toward recognising its metabolic and non-communicable nature. SLD encompasses metabolic dysfunction-associated steatotic liver disease (MASLD, defined by the presence of hepatic steatosis together with at least one cardiometabolic risk factor and low or no alcohol intake), metabolic dysfunction- and alcohol-associated liver disease (MetALD, defined by moderate alcohol consumption of 140–350 g/week in females and 210–420 g/week in males), and alcohol-associated liver disease (ALD defined by excessive alcohol consumption of ≥350/420 g/week in females/males, respectively).[1] Given the dynamic nature of SLD, driven by fluctuations in alcohol consumption and metabolic factors, regular re-evaluation is required to maintain appropriate classification and to guide prevention, treatment, and care.[2]

MASLD accounts for the majority of SLD cases and has become one of the leading causes of cirrhosis, hepatocellular carcinoma (HCC), and liver transplantation.[3] Driven by the parallel global rise in obesity and type 2 diabetes (T2D) in adults, as well as increasing metabolic dysfunction in younger populations, MASLD has emerged as a major public health challenge. Its growing burden is associated with increased liver-related morbidity, rising healthcare costs, and reduced quality of life.[4,5] Global estimates indicate that approximately one-third of adults worldwide have MASLD, with a pooled prevalence of 32.4%, while around 5% have metabolic dysfunction-associated steatohepatitis (MASH).[6,7] The global prevalence of MASLD in children and adolescents is also increasing, with estimates at around 13%.[8] MASLD is typically asymptomatic in its early stages and progresses slowly, but its course can accelerate in the presence of indicator conditions, including T2D, obesity, and clustering of cardiometabolic risk factors. The pathophysiology of MASLD reflects the interplay between metabolic dysregulation, genetic susceptibility, lifestyle behaviours and metabolic exposures, including alcohol intake, all of which contribute to disease progression and fibrosis risk.[3,9] Fibrosis stage remains the strongest predictor of liver-related outcomes and has become a central target

Key messages

- Steatotic liver disease remains widely underdiagnosed and non-invasive tests for fibrosis assessment are inconsistently applied in primary care, leaving many individuals unidentified until cirrhosis or complications develop.
- Risk-stratified, sequential diagnostic strategies, including timely access to guideline-recommended second-line tests, improve detection of significant/advanced fibrosis, reduce misclassification, optimise resource utilisation, and accelerate linkage to care.
- In individuals with metabolic indicator conditions for SLD such as T2D, obesity, or multiple cardiometabolic comorbidities, the higher pre-test probability of advanced fibrosis may justify earlier access to higher-performing guideline-recommended second-tier tests, rather than starting with a FIB-4 test.
- Structured multidisciplinary models of care linking primary care, hepatology, endocrinology, diabetology, cardiology, obesity medicine and mental health services can improve coordination, reduce fragmentation, and support timely fibrosis detection and longitudinal management.
- Laboratory-enabled diagnostic strategies, including automated fibrosis scoring and reflex testing, offer scalable opportunities to increase case-finding and improve referral efficiency, but require alignment with local health system capacity, workforce availability, and reimbursement frameworks.
- Supported by digital tools, artificial intelligence, and policy integration, fibrosis-focused diagnostic approaches can strengthen liver health within broader metabolic and non-communicable disease frameworks and support a shift toward proactive population-based care.

for risk stratification, treatment eligibility, and longitudinal monitoring.[10,11] This reinforces the importance of adopting a structured and coordinated approach spanning risk identification, fibrosis assessment, referral, treatment, long-term follow-up and support. Together, these interconnected steps define the continuum of care for SLD.[12,13]

Lifestyle modifications aimed at achieving clinically significant weight loss remain the cornerstone of managing MASLD.[3] However, in real-world settings, only a minority achieve and maintain the degree of weight loss required for meaningful histological improvement through lifestyle changes alone.[14] Although liver biopsy remains the reference standard for diagnosing MASH and staging fibrosis, its invasiveness, cost, and sampling variability limit its routine use. Blood- and imaging-based non-invasive tests (NITs) are now accepted as feasible alternatives for fibrosis assessment, risk stratification, and longitudinal monitoring in SLD, with the Food and Drug Administration (FDA) encouraging the development of evidence supporting NITs as "reasonably-likely surrogate endpoints (RLSE)".[15,16] Recent therapeutic advances, including the approval of the first two agents for non-cirrhotic MASH with moderate to advanced fibrosis (F2–F3) by the FDA in 2024 and 2025 (resmetirom and semaglutide), and the approval of resmetirom in the European Union (EU) in 2025, have increased the urgency for reliable and scalable diagnostic pathways capable of supporting treatment eligibility and follow-up. This reinforces the central role of NITs within contemporary SLD care.[17,18]

Improving fibrosis assessment across the continuum of care for SLD requires appropriate diagnostic tools together with stronger coordination across specialities.[19,20] Engaging primary care providers (PCPs), people with lived experience, and structured models of care (MoCs), supported by digital infrastructure, is essential to address gaps in early identification and equitable access to fibrosis assessment.[20] Recent advances in laboratory automation, including reflex testing, and the integration of electronic health records (EHRs) with artificial intelligence (AI), offer opportunities to identify people with undiagnosed fibrosis beyond specialist settings and support active case-finding strategies.[3,12]

In this Series paper, we examine diagnostic innovations and emerging MoCs to improve risk stratification and fibrosis assessment across the continuum of care for SLD, with a focus on scalable, population-oriented strategies to support equitable liver health delivery across Europe.

Gaps in fibrosis assessment across the continuum of care for SLD

In MASLD, risk identification typically takes place in primary care settings, particularly for people living with obesity, T2D, or metabolic syndrome (MetS), but should also be integrated into routine assessment across non-liver specialities (e.g., endocrinology, diabetology, and cardiology) within metabolic care pathways.[12,19] In MetALD and ALD, risk identification often occurs in primary care, substance use, or internal medicine settings.[21] In this context, systematic screening for harmful alcohol consumption is a key component of risk identification. Validated tools such as the Alcohol Use Disorders Identification Test (AUDIT) can support the identification of individuals at risk of ALD and MetALD across care settings.[21] Nevertheless, many individuals with SLD remain

undiagnosed, due to limited awareness, restricted access to care, and inconsistent testing practices.[22] Once individuals at risk have been identified through case-finding approaches, NITs are used to stratify fibrosis risk and disease severity, primarily by excluding advanced fibrosis. Additionally, when clinically indicated, alcohol consumption can be assessed using biomarkers such as phosphatidylethanol (PEth).[21,23] Subsequent management focuses on structured lifestyle changes, optimisation of cardiometabolic risk factors, and, when indicated, referral for specialist evaluation and liver-specific pharmacotherapy.[15] Lifestyle interventions should be delivered longitudinally and integrated within multidisciplinary care, given their central role across all stages of disease. Long-term follow-up requires monitoring of disease progression, support with treatment adherence, and coordination across specialities.[24]

Several interrelated barriers along the continuum of care for SLD hinder early fibrosis detection, coordinated management, and long-term follow-up (Fig. 1). One of the major challenges is delayed fibrosis detection, as SLD often remains asymptomatic for many years and many individuals remain undiagnosed until cirrhosis or HCC develops, stages at which identification of SLD as the underlying aetiology may be challenging, as hepatic steatosis often declines with the evolution of more fibrotic disease, leading to a "burnt-out" phenotype.[25] PCPs often take a reactive approach to liver disease, acting only when abnormal blood test results or late-stage symptoms appear.[25] Consequently, proactive case-finding initiatives remain uncommon, and detection rates are low outside a limited number of 'bright-spots' where automated liver testing algorithms have been implemented.[26,27] Even simple, low-cost scores such as the Fibrosis-4 (FIB-4) index are underused due to poor workflow integration, lack of automated calculation, and low familiarity among clinicians.[28,29]

Fragmentation of care further disrupts coordinated fibrosis assessment and longitudinal management. SLD management involves multiple specialities, including primary care, hepatology, diabetology, endocrinology, cardiology, obesity medicine, nutrition, behavioural health, and substance-use services, yet coordination across these domains remains limited.[30] Evidence from European pilot programmes indicates that unclear referral criteria, inconsistent feedback loops, and weak cross-sectoral coordination lead to inefficiencies and high patient drop-out rates.[31] These structural weaknesses also hinder care retention, especially when follow-up responsibilities are transferred between specialities. In addition, the delivery of structured and effective lifestyle programmes is often inconsistent or absent, further limiting the translation

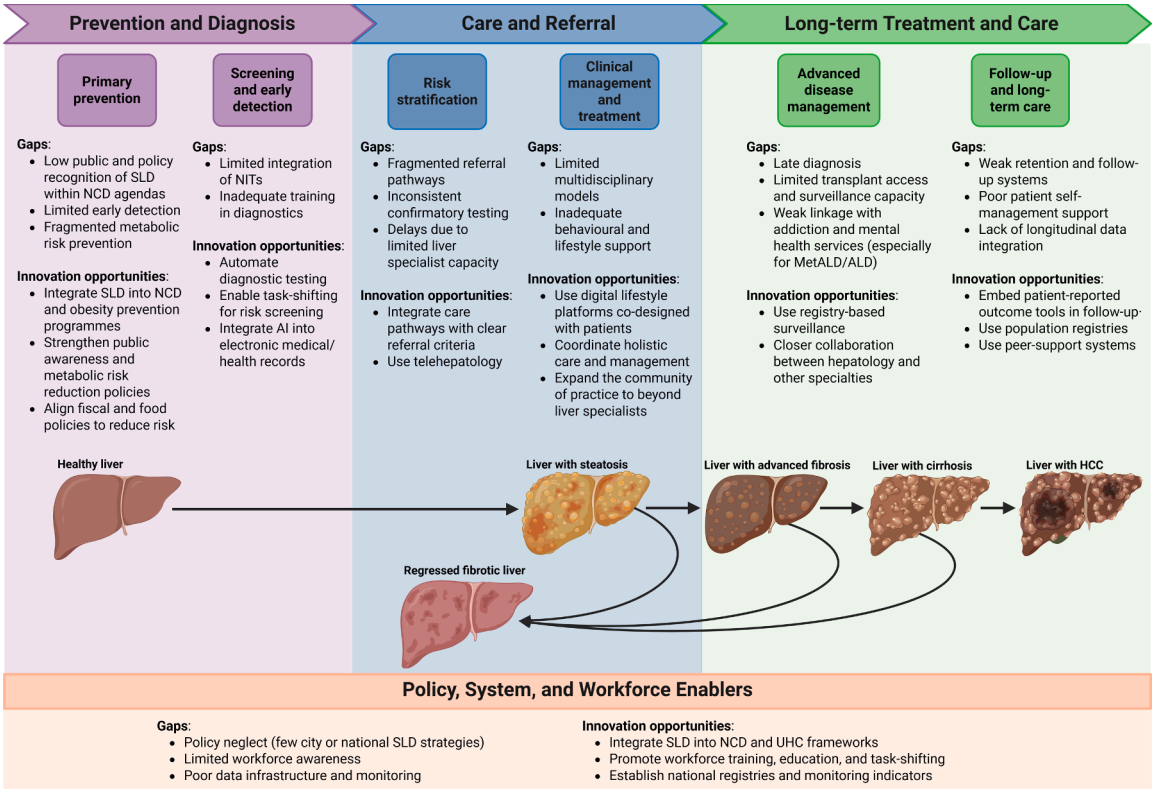

Fig. 1: Key gaps and innovation opportunities across the steatotic liver disease continuum of care.

of guideline recommendations into sustained behavioural change. These factors can result in real-world attrition across the continuum of care, including missed case identification, delayed referral, and loss to follow-up, ultimately reducing the population-level effectiveness of otherwise validated diagnostic strategies.[32]

These challenges are exacerbated by time constraints, staff shortages, financial limitations, and a lack of training in the management of liver disease among non-hepatology specialists, as well as ongoing policy neglect.[33,34] Despite the growing burden of disease, few countries incorporate SLD into national non-communicable disease (NCD) strategies. This policy gap perpetuates underfunding, fragmented service delivery, and inconsistent implementation of structured MoCs.[35]

These barriers highlight the pressing need for scalable diagnostic strategies and integrated MoCs to improve fibrosis assessment and equitable risk-stratified care across Europe, particularly among high-prevalence groups such as people living with T2D and/or obesity.[32]

Diagnostic innovation for early fibrosis detection

Non-invasive tests and blood-based biomarkers

Abdominal ultrasound remains the most used first-line imaging modality for investigating the cause of abnormal liver function tests and thereby for the detection of hepatic steatosis among individuals at risk, or with suspected chronic liver disease. However, its inability to reliably stage liver fibrosis, in the context of rising global rates of MASLD, underscores the central role of NITs in fibrosis assessment and risk stratification.[3,15] Although there is a growing enthusiasm for technological solutions, their integration into routine non-specialist care is limited. Diagnostic innovation increasingly incorporates AI into fibrosis case-finding and risk stratification, but these approaches currently complement rather than replace guideline-established NIT-based diagnostic strategies.[36] Although most evidence derives from MASLD, these strategies are increasingly relevant across the wider SLD spectrum, including MetALD and ALD, where early detection of liver fibrosis is often more challenging due to fluctuating alcohol intake, stigma and low screening rates.[21] Blood- and imaging-based NITs enable scalable assessment of significant/advanced liver fibrosis across care settings, supporting task-shifting from specialists to primary care, allied healthcare professionals (HCPs), and laboratories.[26] Blood-based NITs include indirect biomarkers, which estimate liver fibrosis using routine laboratory parameters, and direct biomarkers, which reflect extracellular matrix turnover.[15,16]

Indirect tests, such as FIB-4, NAFLD Fibrosis Score, and AST-to-Platelet Ratio Index (APRI) are widely used as first-line tests because of their low cost and broad availability.[15,16] Among these, FIB-4 has emerged as the most widely recommended due to its simplicity and increasing integration into automated laboratory and electronic health record pathways.[15] However, its performance varies according to disease prevalence and population characteristics.[37,38] Additional indirect scores, including SAFE, LiverPRO, and LiverRisk, have been recently developed to further improve risk stratification.[39,40]

Age-independent NITs developed from population cohorts, such as the Metabolic Dysfunction-Associated Fibrosis 5 (MAF-5) score, have demonstrated improved accuracy for fibrosis assessment and prediction of liver-related events.[41] However, their implementation remains limited, partly due to the absence of automated calculation and integration within EHR and laboratory workflows.[32] In parallel, newer prognostic approaches aim to estimate the future risk of cirrhosis or liver-related events. For example, the Cirrhosis Outcome Risk Estimator has shown improved performance compared with FIB-4 for predicting future liver-related events.[42] However, the role of such prognostic models compared to currently used diagnostic models remains to be clarified.

Direct serum biomarkers such as the Enhanced Liver Fibrosis (ELF) test provide more accurate fibrosis assessment and staging and are increasingly used as second-line tools after FIB-4. However, reimbursement limitations and laboratory constraints continue to restrict uptake across most health systems.[15,29,43,44] Imaging-based NITs, particularly VCTE, have become central to the assessment of liver fibrosis due to their reproducibility and prognostic relevance.[45] Magnetic resonance elastography (MRE) is the most accurate non-invasive modality, but its high cost, technical demands, and limited availability continue to restrict its use primarily to specialist or research settings.[46]

The most effective strategy for early detection of clinically significant fibrosis is sequential use of serum and imaging tests within risk-stratified approaches, supporting direct access to second-line testing in high-risk groups with indicator conditions, rather than mandating FIB-4 as the universal initial step.[47] In high-risk populations, including individuals living with T2D, obesity, or multiple metabolic comorbidities, reliance on indirect scores alone may reduce diagnostic accuracy and lead to both underestimation of fibrosis and increased costs due to unnecessary testing triggered by false-positive results and missed diagnoses in those with false-negative results.[38,48] This underscores the importance of not using indirect scores as the sole NIT in these groups when the test is negative.

Within sequential care pathways, low-risk results generally support continued management in non-specialist settings with periodic reassessment. However, intermediate-risk findings, which account for a substantial proportion of cases in real-world practice,

often lead to referral to specialist care, increasing demand on hepatology services. This highlights the need for more accurate first-line risk stratification and automated triage strategies to better target specialist resources.[40] Risk-stratified pathways improve the detection of significant fibrosis and reduce misclassification. Longitudinal studies further indicate that sequential pathways also provide prognostic stratification, identifying people at increased risk of liver-related events.[49]

Non-invasive diagnostic approaches discussed in this Series paper are summarised in Supplementary Table S1.

Technology-enabled strategies for fibrosis case-finding and risk stratification

Although NITs are fundamental to current diagnostic strategies, technological advances, including PoC devices, automated laboratory workflows, and AI-driven algorithms, provide additional opportunities for fibrosis case-finding in non-specialist settings.[12,36] PoC diagnostics, particularly portable imaging, enable fibrosis assessment closer to routine care and have demonstrated improved triage accuracy in primary and community care settings, facilitating identification of individuals who truly require specialist referral.[50] Task-shifting, including nurse-led delivery of imaging, further enhances diagnostic access, particularly in resource-constrained health systems.[51]

Automated, laboratory-based diagnostic pathways represent another critical strategy for improving early fibrosis detection.[52,53] In Scotland, the University of Dundee's implementation of intelligent liver function testing (iLFT) programme integrates automated algorithms into regional laboratory systems to evaluate abnormal liver function tests.[26] By combining minimal clinical information (body mass index [BMI], alcohol intake, and MetS status) with reflex testing for common liver diseases, iLFT generates a probable diagnosis and management plan that is returned directly to the referring clinician. Evaluations based on data from 28,000 implementations have demonstrated improved diagnostic efficiency, workflow integration, and referral optimisation.[26]

Although automated approaches can improve the consistency and scalability of case-finding, implementation without appropriate clinical context and predefined action thresholds may increase the risk of overdiagnosis.[54] Therefore, automation should be embedded within protocol-driven, stepwise diagnostic approaches that include confirmatory second-line testing and linkage to proportionate management to maximise benefits while minimising risks.[54]

Proprietary tools such as LiverPRO illustrate the potential of automation within structured care pathways. LiverPRO is a CE-marked in-vitro medical software tool designed to identify individuals at risk of ≥F2 fibrosis using combinations of routine biochemical variables and age.[55] Developed and validated in large European cohorts, its performance has been shown to be comparable to established second-line tests and superior to commonly used first-line scores.[55]

Beyond laboratory-based automation, digital technologies, including AI, can further expand community-level risk stratification.[56] These models integrate clinical, biochemical, and sociodemographic variables to identify individuals who may benefit from fibrosis assessment and further evaluation and can be embedded within clinical decision-support systems.[56] Emerging digital tools, including wearable devices and mobile health applications, provide additional opportunities for risk identification.[36] Studies using wearable devices have demonstrated an inverse relationship between physical activity and incident chronic liver disease. Pilot clinical studies also suggest that digital biomarkers such as physical activity, sleep patterns, and heart rate variability, may provide insight into individual metabolic risk profiles. However, MASLD-specific evidence remains preliminary.[36,57] Mobile health applications allow users to self-report diet, alcohol consumption, and lifestyle behaviours. Combined with wearable-derived metrics, these platforms can generate integrated digital biomarkers that support fibrosis-focused risk identification within SLD care.[36] Telemedicine and remote monitoring systems can further improve access for rural or underserved populations by enabling virtual consultations, and home-based assessments.[58]

Future directions in fibrosis diagnostics

The next generation of fibrosis-focused diagnostic innovation is emerging from molecular profiling, quantitative imaging, and AI. These tools are expected to augment current stepwise diagnostic approaches. Omics and sequencing technologies are creating new opportunities to identify individuals at risk of progressive fibrogenesis through integration of genomic, proteomic, and metabolomic data.[59] However, many omics platforms show high analytical variability and limited standardisation.[59] Polygenic risk scores (PRSs) may improve MASLD risk stratification. Combining PRSs with clinical parameters may enhance early detection and further improve fibrosis prediction.[60] Beyond PRSs, targeted protein biomarkers (e.g., collagen neo-epitopes such as propeptide of type III collagen [pro-C3]) and multi-analyte panels provide additional indicators of active hepatic fibrogenesis. Emerging signals include cell-free DNA methylation, extracellular vesicles, microbiome signatures, and breathomics.[59,61] Cross-platform harmonisation, validation across diverse ancestries, and demonstration of incremental value over existing NITs remain key unmet needs.

Imaging technologies are advancing toward the direct quantification of fibrosis. Quantitative magnetic

resonance imaging (MRI)-based methods, such as iron-corrected longitudinal relaxation time constant (T1) mapping and MRE, provide reproducible and operator-independent assessments of disease activity, outperforming VCTE in the detection of significant liver fibrosis.[46] AI offers further opportunities to improve the detection of fibrosis from imaging data. Convolutional neural networks, when trained on ultrasound, computed tomography, or MRI data, can enhance image quality and detect early fibrosis changes. Nevertheless, variations in scanners and acquisition protocols limit reproducibility, confining these approaches largely to research settings.[36,46]

Despite the growing promise of omics-based and AI-augmented diagnostics, none of these tools is yet ready for clinical adoption within early fibrosis detection strategies. Implementation will require large-scale validation, technical standardisation, and robust cost-effectiveness evaluation. Nevertheless, these advances lay the groundwork for precision hepatology, in which early identification of liver fibrosis risk may enable timely and personalised intervention.

Integrated models of care for fibrosis detection and risk stratification

Although international guidelines recommend case-finding in high-risk groups (e.g., people living with T2D and/or obesity), implementation remains limited in Europe.[15] Most health systems still rely on siloed care pathways with limited coordination between specialities, resulting in under-identification of individuals at risk of liver fibrosis and gaps in care.[19,24,25] Integrating systematic fibrosis assessment into primary care follow-up for chronic diseases such as T2D, obesity, and CVD can support earlier identification of individuals with MASLD at risk of clinically significant fibrosis.[24] Similarly, embedding alcohol-risk assessments and standardised approaches for MetALD and ALD within primary care and substance use services remains essential but inconsistently implemented.[21] Digital tools and reflex testing algorithms can support triage and reduce unnecessary referrals to liver specialists, strengthening the role of primary care and preserving specialist capacity for advanced disease (Fig. 2).[26,27,62]

Multidisciplinary, protocol-driven MoCs are essential for scalable disease management.[24] SLD, particularly MASLD, is increasingly recognised as a systemic condition that requires MoCs moving beyond a traditional organ-specific approach.[3,15] Clinics in which hepatology, endocrinology, cardiology, internal medicine, nutrition, laboratory medicine, obesity medicine and primary care collaborate under shared protocols, rather than working in discrete silos, can improve risk assessment and linkage to care while reducing duplication of tests and consultations.[24] Such models enable coordinated assessment of cardiometabolic risk and liver fibrosis within a single care pathway. Within these settings, nurse-led pathways incorporating lifestyle counselling and targeted NITs, such as VCTE, can facilitate earlier identification of significant liver fibrosis while supporting patient education and lifestyle modifications.[51,62] For individuals living with MetALD or ALD, integration of hepatology with addiction medicine, mental health services, and social support is critical to ensure continuity of care.[21]

Digital infrastructure amplifies the effectiveness of integrated MoCs. Clinical decision support systems, shared registries, and telemedicine improve coordination, facilitate surveillance, and maintain linkage to care, particularly in underserved areas.[58] Community-based strategies, including mobile assessment units, primary care outreach, and involvement of individuals with lived experience, can additionally reduce stigma, improve engagement, and promote more equitable access to liver health services.[63]

Crucially, diagnostic pathways should be tailored to target populations. Clinical risk profiles, ethnicity, socioeconomic factors, geographical access, and health system capacity can all influence the effectiveness of diagnostic strategies.[19] Consequently, these strategies may perform differently across settings and populations. In settings with limited resources, scalable approaches such as the use of low-cost, first-line NITs and laboratory-enabled strategies may facilitate implementation and reduce reliance on specialist models.[19]

Barriers to diagnostic implementation across the continuum of care for SLD

A key challenge in the implementation of diagnostic strategies for SLD lies in how NITs are conceptualised and applied across clinical settings. Many tools were developed for specific purposes and populations but are often used interchangeably beyond their original validation. This mismatch between development and real-world application can complicate interpretation and, in certain contexts, increase the risk of inappropriate clinical inference. In addition, many scores rely on the same routine laboratory variables, meaning that apparent diversity often masks substantial methodological overlap, limiting the incremental information provided by each test, and contributing to variability in downstream decision-making when applied outside their derivation populations. This overlap may also introduce circularity when analytes used to define or select study populations are incorporated into the composite NITs subsequently evaluated.[3,37,38]

Beyond these conceptual limitations, several system-level barriers hinder the implementation of technology-enabled case-finding strategies. HCPs may be reluctant to adopt new digital tools because of limited training, lack of trust, or concerns about workload.[64] In many settings, algorithms often require manual entry of clinical variables outside the electronic health record, increasing the risk of error and compromising data

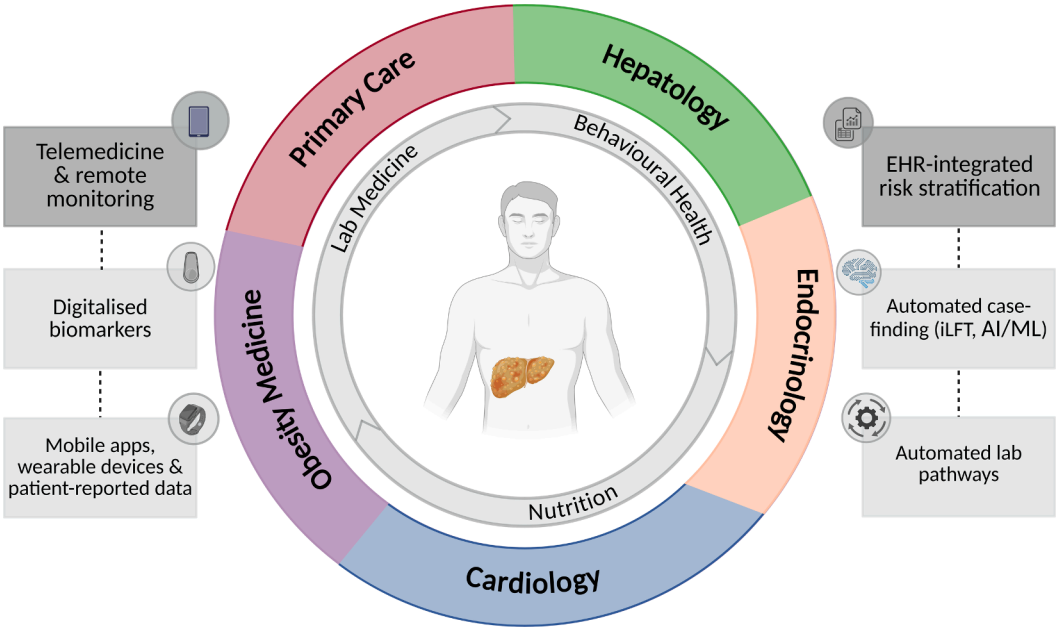

Fig. 2: Integrating digital health tools into multidisciplinary SLD models of care.

integrity. Poor interoperability between electronic health records, laboratory information systems, and primary care software further constrain implementation.[64]

Laboratories play a central role in automated diagnostic pathways, as demonstrated in Scotland, with automated all-cause liver function testing, and regions in Hong Kong, Malaysia and Spain, implementing automated FIB-4 calculation.[12,27] However, many laboratories lack the hardware, information management systems, and clinical order communication infrastructure required for full automation. Implementation often requires additional investments, including software licencing, equipment, and integration of reflex testing.[56] Reimbursement policies frequently fail to account for the operational and financial implications of automated analyses, further limiting scale-up.[56]

Regulatory and policy barriers add further complexity. In the European Union, diagnostics must comply with the 2021 In Vitro Medical Device Regulation with additional national approval requirements in some countries. Funding constraints remain substantial, as health system budgets are commonly organised in operational silos and tend to prioritise short-term objectives over long-term investments in prevention and early detection.[32,56]

Real-world evidence highlights how these conceptual and system-level barriers translate into practical implementation challenges. A 2024 study in Germany, Italy and the United Kingdom found that physicians managing high-metabolic-risk populations reported limited knowledge of NITs, partly due to the lack of clear referral pathways between primary and specialist care.[65] Similarly, a pilot study involving three US healthcare systems revealed that, while provider confidence increased following exposure to a structured MASLD model of care, operational barriers included insufficient training, manual calculation of FIB-4, limited EHR integration for VCTE ordering, and reimbursement uncertainty.[31]

Structural and societal barriers further exacerbate inequities in access to timely detection. The magnitude and relative importance of these barriers vary across countries and health systems, reflecting differences in workforce capacity, reimbursement, digital infrastructure and the organisation of care. Reimbursement for serum-based fibrosis panels and VCTE varies widely across Europe, limiting their use in community and primary care settings.[66] More broadly, the real-world impact of diagnostic innovations depends on more than just technical performance. Reach, affordability, and equitable access are equally critical, as highly accurate tools may still have limited population-level benefits if access to these tools is constrained by cost, infrastructure or workforce capacity. Socioeconomic deprivation and stigma related to metabolic risk reduce engagement with screening, disproportionately affecting vulnerable populations.[67,68] Among individuals living with alcohol use challenges or ALD/MetALD, additional stigma and fragmented substance use pathways further impede early fibrosis detection.[21] In addition, the feasibility of task-shifting strategies, including nurse-led delivery of diagnostic tests such as VCTE, is highly context-dependent. In some healthcare systems,

Panel 1: **Recommendations**

1. **Invest in scalable, automated non-invasive diagnostics**
   - Support reimbursement and implementation of validated NITs, prioritising automated laboratory-enabled strategies and digital decision-support tools for primary care professionals.
   - Establish clear guidance on first- and second-line NITs, and distinguish targeted case-finding in high-risk groups from population-level screening.
2. **Expand integrated, digitally enabled models of care**
   - Fund coordinated pathways that combine primary care-led triage, telemedicine, and task-shifting (including nurse- and operator-led VCTE), and interoperable digital tools, to improve care access and reduce specialist burden.
3. **Address equity across gender, ethnicity, geography, and resource settings**
   - Prioritise mobile- and community-based diagnostics for rural and low-resource areas.
   - Policies should explicitly account for gender and gender-diverse populations, and strengthen care access for populations affected by stigma, including those living with alcohol use challenges.
   - Adopt proactive approaches to understanding the limitations of NITs across ethnic groups.
4. **Build workforce capacity for timely detection**
   - Invest in training primary care, endocrinology, cardiology, and obesity specialists, in addition to laboratory medicine professionals, in the use and interpretation of NITs and in structured referral systems, with endorsement from professional health associations.
5. **Harmonise regulation and accelerate validation of innovations**
   - Align EU and national regulatory pathways and support multi-country validation of digital and novel diagnostics, while generating cost-effectiveness evidence to inform the sustainable reimbursement of these innovations.
6. **Integrate liver health into metabolic non-communicable disease strategies**
   - Embed MASLD/MASH detection into diabetes, obesity, and cardiovascular clinical and research programmes.
   - Recognise liver fibrosis assessment as a core metabolic risk indicator and promote metabolic multidisciplinarity across hepatology, endocrinology, including diabetology, obesity medicine, and primary care.
   - Include steatotic liver disease in city, national and EU-wide NCD action plans and strategies.

shortages of nursing can limit scalability as much as shortages of physicians, highlighting the need for locally adapted workforce planning.[69]

Addressing these barriers requires coordinated, cross-sector collaboration. Successful implementation of diagnostic innovation depends on close co-design between primary and secondary care, laboratories, and health system stakeholders, supported by interoperable digital infrastructure and clear referral pathways. The presence of respected local champions has repeatedly been identified as a key facilitator of implementation.[56]

In response to these challenges, multi-country initiatives are emerging across Europe. The LIVERAIM and Global Research Initiative for Patient Screening on MASH (GRIPonMASH) projects aim to identify effective, feasible, and economically sustainable strategies for early SLD identification, integrating blood-based biomarkers with digital and AI-driven risk stratification and supporting large-scale, multi-country validation.[70,71]

Implementation, policy alignment, and future research priorities

Although MASLD reflects systemic metabolic dysfunction, it remains insufficiently integrated into broader chronic disease and NCD strategies. The liver acts as a marker of metabolic imbalance, yet indicators of liver health are rarely incorporated into frameworks for obesity, T2D, or CVD.[12] Aligning MASLD with these established infrastructures represents a pragmatic implementation strategy, enabling earlier identification of individuals at risk without creating new programmes.[19,72] Emerging frameworks, such as the cardiovascular-kidney-metabolic health model proposed by the American Heart Association, as well as the recently developed cardiovascular-liver-metabolic health concept generated through multidisciplinary consensus, illustrate how liver health could be integrated into NCD prevention strategies.[73]

At the policy level, however, MASLD remains underrecognised.[35] For instance, the draft political declaration for the Fourth United Nations High-Level Meeting on NCDs (September 2025) used the outdated terminology and addressed NAFLD mainly in relation to liver cancer prevention, missing the opportunity to position liver health as a cross-cutting metabolic priority.[72] However, calls for a World Health Assembly resolution are now being advanced with the WHO Executive Board in February 2026 agreeing to put forward a resolution on steatotic liver disease. The resolution calls for incorporating liver health metrics into NCD strategies, which could translate diagnostic innovation into practice by supporting structured risk stratification, defined referral thresholds, and coordinated follow-up across

Search strategy and selection criteria

We searched PubMed/MEDLINE for English-language publications up to October 2025 using combinations of terms related to steatotic liver disease, metabolic dysfunction-associated steatotic liver disease, metabolic dysfunction-associated steatohepatitis, alcohol-associated liver disease, metabolic dysfunction- and alcohol-associated liver disease, non-alcoholic fatty liver disease, and non-alcoholic steatohepatitis, together with keywords related to liver fibrosis, screening, non-invasive tests, biomarkers, imaging, point-of-care diagnostics, digital tools, diagnostic pathways, and models of care. We also reviewed relevant international and regional guidelines and policy documents. We prioritised studies addressing early fibrosis detection, diagnostics, and integrated or multidisciplinary care pathways, with particular attention to evidence generated in Europe. The aim of this paper is not to provide a comprehensive review of all available non-invasive tests. Instead, selected approaches are discussed as illustrative examples, based on their validation status, clinical relevance, and feasibility of implementation across health systems.

care levels. Promoting liver health as a measurable component of metabolic well-being would also improve policy coherence, facilitate resource allocation for multidisciplinary MoCs, and reinforce liver injury and fibrosis risk as early markers of metabolic deterioration.[74]

A key challenge in the management of SLD is the limited durability of benefits once lifestyle or pharmacological interventions are discontinued.[13,17] This underlines the need for studies on long-term maintenance strategies, sequential treatment approaches, and scalable MoCs. In particular, clearer definitions are needed on how NITs should guide treatment decisions, intensity of follow-up, and monitoring of responses over time. As most individuals living with MASLD will not progress to advanced liver disease, research priorities should focus on generating real-world evidence to identify those at the highest risk for disease progression, evaluate digitally supported lifestyle and metabolic management models, and assess the cost-effectiveness of diagnostic and therapeutic pathways on a large scale.[26,48]

Medical laboratories represent a major opportunity for scalable case-finding. Experience from Scotland illustrates how laboratory medicine can embed automated risk stratification into routine workflows, facilitating earlier identification while preserving specialist capacity.[26] In health systems facing workforce constraints in primary and specialist care, laboratory-enabled pathways provide a concrete implementation lever, supporting task-shifting while maintaining diagnostic quality. When combined with predefined thresholds and structured feedback to non-specialist providers, laboratory-driven outputs can reduce unnecessary referrals, streamline specialist workload, and enable the integration of liver-specific care into routine clinical practice.[75] Examples of best practice demonstrate how laboratory-enabled pathways can improve efficiency in generalist and specialist settings, reduce overall system costs, and improve outcomes for individuals living with SLD and related comorbidities.[75]

Together, these developments highlight a pivotal opportunity for liver health. By embedding MASLD within broader metabolic and NCD frameworks, strengthening laboratory-enabled early detection, and investing in sustainable MoCs, health systems may transition from fragmented and reactive management to a proactive, equitable, and population-based approach. Such an approach should facilitate diagnostic innovation and meaningful improvements in fibrosis detection, risk stratification, and coordinated care across the continuum of care for SLD.

Conclusions

Europe must shift from reactive, specialist-dependent care toward a proactive, system-wide approach across the continuum of care for SLD, centred on timely and accurate fibrosis assessment, coordinated interventions, and risk-stratified management. The integration of liver fibrosis assessment and reflex testing algorithms into laboratory workflows or EHR systems offers one of the most scalable strategies to improve early fibrosis detection. In individuals with indicator conditions such as T2D and obesity, earlier access to more accurate, guideline-recommended NITs, particularly ELF and VCTE within risk-stratified strategies, may reduce false negatives, improve triage efficiency, and accelerate linkage to care.

Promoting liver health as a measurable component of metabolic well-being would also improve policy coherence, support resource allocation and multidisciplinary models of care, while reinforcing liver fibrosis risk as a measurable marker of metabolic deterioration within integrated care pathways. Translating diagnostic innovation into standard care requires coordinated European action. This should be supported by robust frameworks such as the European Health Data Space Regulation, to align education, digital infrastructure and policy. Closing systemic gaps across the continuum of care for SLD is essential to translate diagnostic innovation from research settings into equitable, real-world public health impact and durable improvements in fibrosis detection and risk-stratified care (see Panel 1).

Contributors

NP, TMW, PNB, CDB, and JVL conceived the manuscript. All authors participated in drafting the first version of the article and reviewed and approved the final version.

Declaration of interests

NP has served as a speaker or advisor for Gilead, Gore, AstraZeneca, and Novo Nordisk and has received travel grants from Gilead and AbbVie, outside of this work.

TMW has received payment by the Pasteur Institute for a lecture; he has served as an unpaid fellow for the UNITE Global Health Parliamentarians Network, an unpaid member of the Consortium of Universities in Global Health Research Committee and an unpaid mentee for the European Association of the Liver (EASL) Mentorship Program.

PNB has received consultation fees from Resolution Therapeutics, Madrigal, and Novo Nordisk and travel bursaries from Novo Nordisk, outside of this work.

SP acknowledges educational grants to her institutions from Novo Nordisk and Eli LIlly, research grants from Novo Nordisk, Amgen and Structure Therapeutics, consulting fees from Novo Nordisk and Eli Lilly, an unpaid leadership role at the Illinois Obesity Society, and honoraria for promotional lectures from Novo Nordisk, Eli LIlly, outside of this work. She owns Viking Therapeutics. Stock options.

HH's institutions have received research funding from Astra Zeneca, EchoSens, Gilead, Intercept, MSD, Novo Nordisk, Takeda and Pfizer with HH as the PI. He has served as consultant, speaker or on advisory boards for Astra Zeneca, Boehringer Ingelheim, Bristol Myers-Squibb, GSK, Echosens, Ipsen, MSD and Novo Nordisk and has been part of hepatic events adjudication committees for Arrowhead, Boehringer Ingelheim, KOWA and GW Pharma.

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LR-D nothing to declare.

GT nothing to declare.

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JFD nothing to declare.

FT FT's lab has received research grants (funding to the institution) from Astra Zeneca, MSD, Gilead, Agomab. FT has received honoraria for consulting or lectures from Gilead, AbbVie, Falk, AstraZeneca, Boehringer, Mirum, Madrigal, MSD, GSK, Ipsen, Pfizer, Novartis, Novo Nordisk, Sanofi.

CJK nothing to declare.

GS has acted as speaker for Merck, Gilead, AbbVie, Novo Nordisk, Eli Lilly, Lupin, served as an advisory board member for Merck, Novo Nordisk, Gilead, GSK, and has received unrestricted research funding from Novo Nordisk.

JB reports institutional research grants from Diafir, Echosens, Gilead, Intercept, Inventiva, Ipsen, and Siemens, all unrelated to the present work. He has received royalties from Echosens. He has received consulting fees from Boehringer Ingelheim, Novo Nordisk, and Eli Lilly, and speaker honoraria from AbbVie, Echosens, Gilead, Novo Nordisk, Sanofi, and Siemens. He has received support for travel from Gilead. He has served on advisory boards for Lilly, Madrigal, and Novo Nordisk. The author declares no other competing interests.

EAT reports consulting fees from Novo Nordisk, Boehringer Ingelheim, Madrigal, MSD, and Siemens; and speaker or honoraria payments from Novo Nordisk, Boehringer Ingelheim, Echosens, Astra Zeneca, and AbbVie. He has served on an advisory board for GSK. The author declares no other competing interests.

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RV received lecture fees and as a member of advisory boards for Eli Lilly, Novo Nordisk and received research support from Pfizer and AstraZeneca.

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EP declares scientific advisory honoraries for GSK.

SB nothing to declare.

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