



Review Article



# Applications of Artificial Intelligence and Smart Devices in Metabolic Dysfunction-associated Steatotic Liver Disease

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## Abstract

Metabolic dysfunction-associated steatotic liver disease (MA-SLD) is now considered to be among the most prevalent chronic liver diseases worldwide. Its comprehensive management encompasses multiple stages, including risk assessment, early detection, stratified intervention, and long-term follow-up. Among these, improving diagnostic accuracy and optimizing individualized therapeutic strategies remain key challenges in both research and clinical practice. In recent years, artificial intelligence and smart devices have developed rapidly and have gradually been applied in the medical field, offering novel tools and pathways for MASLD risk stratification, non-invasive diagnosis, therapeutic evaluation, and patient self-management. This review summarizes the current applications of artificial intelligence and smart devices in MASLD care, highlights their benefits and limitations, and discusses future directions to support precision diagnosis and treatment strategies.

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## Introduction

Metabolic dysfunction-associated steatotic liver disease (MA-

SLD) is a chronic liver disease marked by the unregulated accumulation of lipids within the liver, which is closely linked to metabolic dysfunction. Patients generally exhibit at least one cardiovascular metabolic risk factor, such as overweight or obesity, type 2 diabetes, or other metabolic abnormalities.<sup>1,2</sup> Epidemiological estimates demonstrate that the global prevalence of MASLD has reached approximately 30% of the adult population.<sup>3,4</sup> MASLD is among the most common chronic liver conditions globally, characterized by a gradual progression that starts with simple steatosis and may develop into steatohepatitis, hepatic fibrosis, and eventually lead to cirrhosis or hepatocellular carcinoma.<sup>5</sup> Timely identification of individuals at elevated risk and the adoption of early, effective therapeutic strategies are critical to halting MASLD progression and enhancing long-term prognoses. MASLD is now recognized as the predominant form of fatty liver disease globally. Strengthening early detection and intervention efforts in this population plays a pivotal role in preventing progression to advanced liver disease and mitigating the overall healthcare burden.<sup>6</sup> The nomenclature of this disease has undergone two significant revisions. In 2020, in light of growing evidence linking obesity and metabolic dysfunction to disease pathogenesis, experts recommended replacing the term nonalcoholic fatty liver disease (NAFLD) with metabolic associated fatty liver disease (MAFLD).<sup>7</sup> Subsequently, in 2023, concerns about the potential stigmatization associated with “MAFLD” led major international hepatology associations to advocate for a further revision, officially renaming the disease as MASLD. This updated terminology reflects a more inclusive diagnostic framework, no longer excluding patients with comorbid chronic liver conditions such as viral hepatitis, alcohol use, or drug-induced liver damage.<sup>2</sup> Epidemiological studies in U.S. adults have reported the prevalence of NAFLD, MAFLD, and MASLD to be 18.5%, 19.3%, and 20.8%, respectively, demonstrating a clear upward trend.<sup>8</sup> Remarkably, approximately 99% of individuals meeting NAFLD diagnostic criteria also fulfill the criteria for MASLD, highlighting a high degree of overlap in their clinical phenotypes. Therefore, findings from previous studies conducted in NAFLD populations remain largely applicable to MASLD research and clinical practice.<sup>9–11</sup>

**Keywords:** Metabolic dysfunction-associated steatotic liver disease; MASLD; Artificial intelligence; Smart device; Diagnosis; Treatment.

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Excessive hepatic fat deposition not only causes direct hepatocellular injury but also induces inflammatory responses, fibrosis progression, and apoptosis. In addition, hepatic insulin resistance further exacerbates lipid accumulation and impairs insulin clearance, ultimately creating a vicious cycle of mutual reinforcement.<sup>12,13</sup> Clinical evidence indicates that individuals with MASLD face significantly elevated risks of cardiovascular disease, with both prevalence and incidence surpassing those seen in the general population.<sup>14</sup> Thus, clinical management of MASLD should emphasize comprehensive control of cardiometabolic comorbidities, including obesity, type 2 diabetes, dyslipidemia, and hypertension, to curb disease advancement and prevent complications.<sup>15</sup> Currently, lifestyle intervention remains the foundational strategy for treating MASLD, encompassing scientifically guided weight loss, balanced diet, and regular physical activity. When necessary, these approaches can be combined with pharmacotherapy or other adjunctive treatments. Additionally, early identification and correction of associated metabolic disorders are crucial steps in preventing disease progression.<sup>16</sup> In recent years, rapid advancements in artificial intelligence (AI) and smart devices have led to their increasing integration into medical practice. Particularly in MASLD research and clinical practice, AI and smart devices have shown great potential in risk prediction, disease screening, auxiliary diagnosis, and personalized treatment. This review synthesizes recent literature from databases including PubMed, Web of Science, and Google Scholar to summarize the current applications and emerging trends of AI and smart devices in MASLD management, aiming to inform and guide future clinical strategies. Furthermore, this review differs from earlier work that mainly focused on imaging. It provides a broader synthesis that links AI algorithms, smart device applications, and ethical considerations across the entire MASLD management pathway.

## Overview of AI and smart devices

AI integrates a multitude of sophisticated algorithms, encompassing machine learning (ML), deep learning, natural language processing (NLP), data mining, and numerous others. ML forms the backbone of this framework. It includes various supervised models such as convolutional neural networks (CNN), decision trees, support vector machines, random forests, and gradient boosting algorithms. In addition, unsupervised, semi-supervised, and reinforcement learning methods are also incorporated (Fig. 1). Deep learning, a major branch of ML, shows particular strength in recognizing complex patterns and handling high-dimensional data.

In medical research and clinical practice, AI is widely applied to the analysis and modeling of multidimensional data based on clinical indicators, biomarkers, and medical imaging, significantly improving early disease detection capabilities, diagnostic accuracy, and the efficiency of personalized treatment decision-making.<sup>17</sup> In disease risk prediction, AI has the capacity to process large-scale patient data to uncover potential risk determinants and estimate the probability of disease development. This facilitates the formulation of individualized preventive strategies tailored to each patient's specific risk profile. In medical imaging recognition, AI enables rapid and accurate detection of underlying pathological features, improving diagnostic efficiency and significantly reducing the risk of human misjudgment. Additionally, in the field of personalized treatment, AI can provide customized therapeutic recommendations based on patients' unique clinical and physiological parameters, thereby enhancing treatment outcomes.<sup>17,18</sup> The application of these technologies not only significantly reduces the time required for traditional data

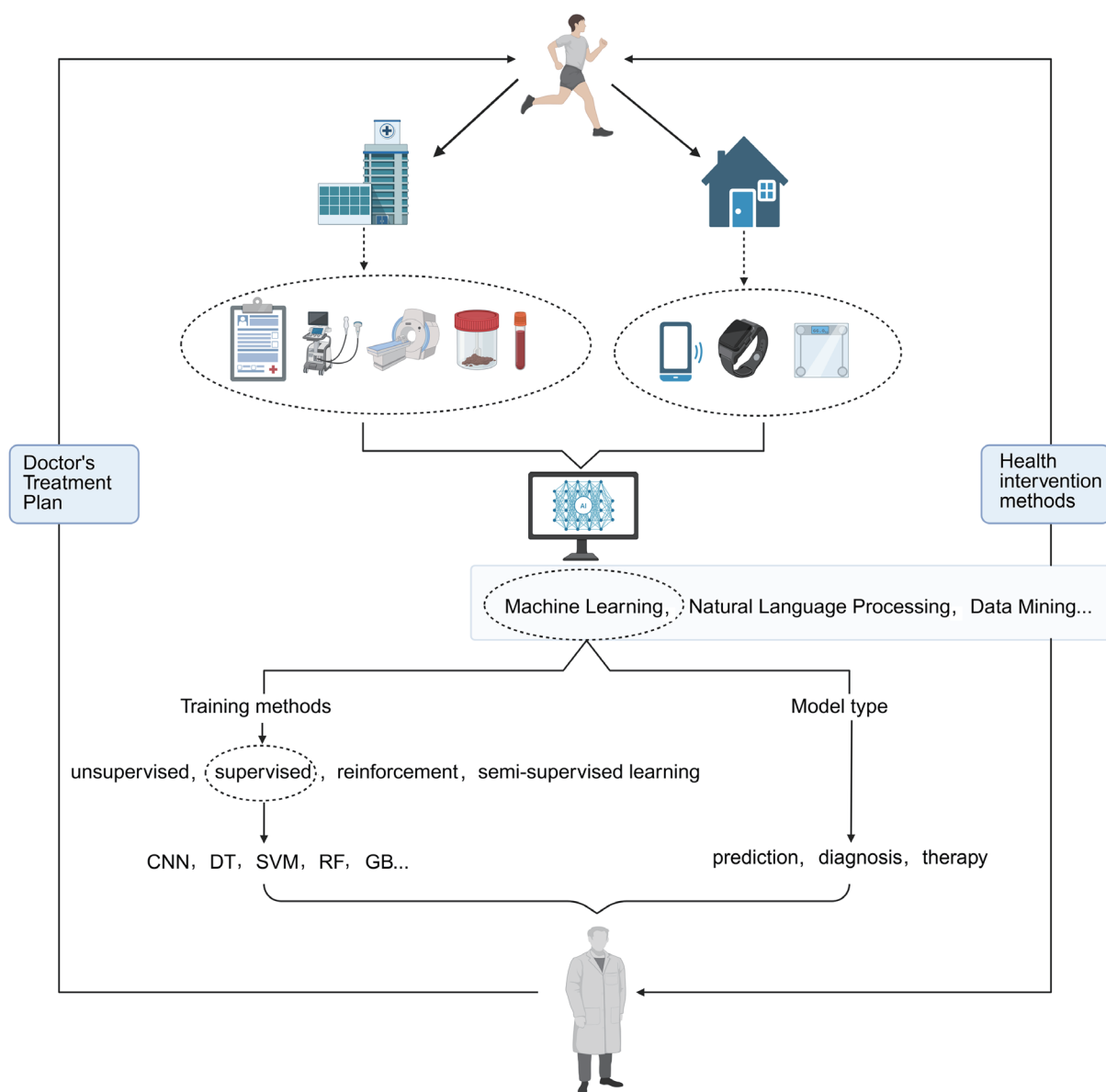
processing and decision-making but also helps overcome subjective biases inherent in human analysis. This demonstrates important potential for managing chronic diseases, including MASLD. Meanwhile, advancements in smart device technology have also provided new tools for health management. Devices such as smartphones, wearables, and portable medical monitors are now equipped with advanced sensors and multimodal data collection capabilities. They can continuously track critical health indicators, including body weight, waist-to-hip ratio, heart rate, glucose levels, and blood pressure. These devices, combined with AI algorithms for data analysis, can provide users with personalized and dynamic health feedback and intervention recommendations. Figure 2 illustrates the application of AI technology and smart devices in managing MASLD: through continuous monitoring and dynamic feedback to enable real-time health tracking and timely adjustment of intervention strategies based on data trends.<sup>19,20</sup>

## Application of AI in MASLD risk prediction and diagnosis

While liver biopsy remains the gold standard for diagnosing steatotic liver disease, its invasive nature, associated bleeding risks, and low patient acceptance restrict its feasibility for widespread use in population-level screening. In recent years, advances in AI technology have brought new breakthroughs in the early screening of MASLD. By synthesizing a broad spectrum of individual data, including clinical metrics such as body mass index (BMI), glucose and lipid profiles, genetic predispositions, and lifestyle habits, AI can establish multidimensional, personalized risk prediction models, significantly improving the efficiency of identifying high-risk individuals. For example, ML applied to large population cohorts can effectively identify high-risk individuals with potential progression from MASLD to metabolic dysfunction-associated steatohepatitis (MASH), thereby enabling the implementation of personalized, stratified intervention strategies.<sup>21</sup> For imaging-based assessments of steatotic liver disease, commonly employed modalities include ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI). Ultrasound is frequently used as a screening method due to its affordability, safety, and non-invasive characteristics. Nevertheless, its diagnostic sensitivity for early-stage or mild steatosis is suboptimal and heavily influenced by operator proficiency. CT can assess the degree of hepatic fat deposition but is susceptible to interference from factors such as iron overload and carries the risk of radiation exposure. MRI, with its high soft tissue resolution and excellent fat quantification capability, is considered the current optimal non-invasive quantitative method, though it is relatively more expensive.<sup>22,23</sup> With the continuous advancement of AI, especially ML and deep learning methods, their application in medical imaging analysis has become increasingly widespread. These AI-driven tools can autonomously derive numerous quantitative imaging features and apply sophisticated algorithms or neural networks to support early diagnosis and treatment tracking of fatty liver disease. Multiple studies have introduced AI-based models for imaging diagnosis of hepatic steatosis. Subgroup analyses reveal that whether employing classical ML techniques or more advanced deep learning architectures, these models demonstrate reliable diagnostic performance across different populations, reference standards, imaging techniques, and transfer learning contexts.<sup>24</sup>

## AI-based predictive models using electronic health records (EHR) and laboratory data

AI shows great promise in processing EHR to construct risk

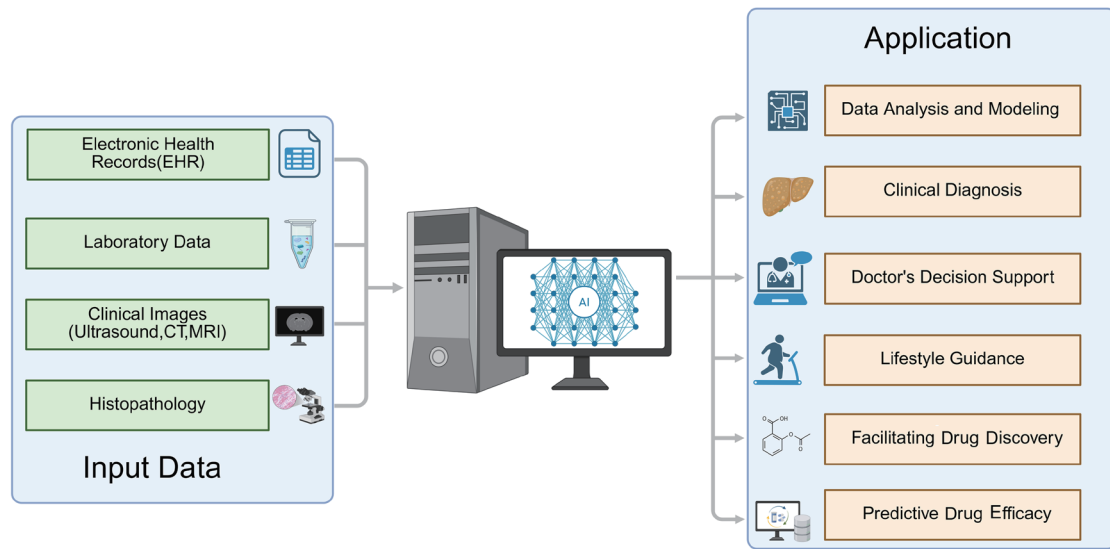


**Fig. 1. The collaborative operation model of artificial intelligence technology and smart devices.** (Created in BioRender). CNN, convolutional neural networks; DT, decision tree; SVM, support vector machine; RF, random forest; GB, gradient boosting.

assessment models for MASLD. With the shift in disease nomenclature from NAFLD to MASLD, whether some non-invasive tests previously used to predict NAFLD remain applicable to MASLD has become an urgent issue in research and clinical practice. Recent studies have shown that certain non-invasive test tools, such as the fatty liver index, still have strong discriminatory efficacy in identifying MASLD risk, suggesting that they retain application value in the new disease classification framework.<sup>25</sup> With the continuous advancement of AI technology, combining non-invasive tests with AI algorithms is anticipated to further streamline MASLD screening workflows—enhancing diagnostic efficiency and reducing the burden on healthcare systems. Currently, commonly used AI methods in EHR-based data analysis include ML, NLP, data mining techniques, and algorithms based on International Classification of Diseases coding. By com-

prehensively analyzing multidimensional information such as demographic characteristics, lifestyle, physical measurements, and laboratory data contained in EHR, AI models can predict the risk of MASLD and assess its severity. Over time, research priorities have clearly evolved. Early studies mainly compared analyses of methodologies. More recent efforts have shifted toward building sophisticated, multimodal predictive systems. For example, Van Vleck *et al.*<sup>26</sup> reported that NLP outperformed text search and ICD coding in identifying MASLD cases from EHR data. Later, Bonfiglio *et al.*<sup>27</sup> developed a model to predict mortality risk, while Yuan *et al.*<sup>28</sup> created a screening tool for younger individuals based on standard physical examination indicators.

A significant step forward is seen in the N3-MASH model proposed by Zhang *et al.*<sup>29</sup> This framework integrates CXCL10 to reflect inflammation, CK-18 to capture apoptosis, and ad-



**Fig. 2. Artificial intelligence and smart devices in clinical management of metabolic dysfunction-associated steatotic liver disease.** (Created in BioRender).

justed BMI as a marker of lipid accumulation. Together, these variables substantially enhance the accuracy of MASH detection. The model marks a transition from dependence on conventional clinical variables to a mechanism-oriented design incorporating novel biomarkers.

Furthermore, the application of AI in multi-omics research is unveiling new insights into disease mechanisms and biomarker discovery. AI technology has also demonstrated broad application value in metagenomics and metabolomics research on various biological samples, especially in identifying potential key genes and biomarkers for MASLD and its different stages of progression. For detailed research results, please refer to Table 1.<sup>21,26,28–34</sup> In genomics and transcriptomics, studies by Conway *et al.*<sup>35</sup> and Park *et al.*<sup>36</sup> have utilized deep learning to identify key genes and signaling pathways, such as the Notch pathway, associated with MASH

severity and hepatic fat accumulation. In metabolomics and lipidomics, the work of teams like McGlinchey<sup>30</sup> and Chiappini<sup>37</sup> has systematically characterized distinct metabolite signatures across disease stages, highlighting the central role of impaired fatty acid metabolism in MASH. Perveen *et al.*'s study, using decision tree analysis, identified high-density lipoprotein levels as an important predictive marker for the development of hepatic steatosis.<sup>31</sup> Additionally, AI-assisted analysis of gut microbiome data highlights the potential of microbial signatures for individualized diagnosis and intervention.<sup>38</sup> More importantly, AI's integrative power is reshaping risk assessment for MASLD. Instead of relying solely on superficial statistical associations, it enables models grounded in biological mechanisms and refined patient subtypes. By combining clinical data with multi-omics information, AI systems can define disease endotypes and guide tailored

**Table 1. EHR and laboratory data**

Author	Country	Year	Categories	Methods	Indicators	Result
Zhang X <i>et al.</i> <sup>29</sup>	China	2025	MASH	N3-MASH	CXCL10, CK-18, BMI	AUC: 0.857
Park IG <i>et al.</i> <sup>32</sup>	Korea	2024	MASLD	SVM,RF,CNN	Genomic DNA	AUC: 0.93
Yuan Y <i>et al.</i> <sup>28</sup>	China	2024	MASLD	Nomogram model	Age, Gender, BMI, Waist-to-hip ratio, ALT, LDL-c, HDL-c, UA, and smoking	AUC: 0.875
McTeer M <i>et al.</i> <sup>21</sup>	UK <i>et al.</i>	2024	MASH	XGBoost	MASLD dataset in Europe	AUC: 0.899
Zhu Q <i>et al.</i> <sup>33</sup>	China	2022	NASH	RF	4 lipid molecules	AUC: 0.923
McGlinchey AJ <i>et al.</i> <sup>30</sup>	Sweden <i>et al.</i>	2022	NAFLD	ML	Clinical data	AUC: F (0–1 vs 2–4) = 0.746, F (0–2 vs 3–4) = 0.778
Kordy K <i>et al.</i> <sup>34</sup>	USA	2021	NASH	RF	Oral and fecal microbiome, plasma metabolites	AUC: 0.99
Van Vleck TT <i>et al.</i> <sup>26</sup>	USA	2019	NAFLD	NLP	EHR	Specificity: 89%, Sensitivity: 93%
Perveen S <i>et al.</i> <sup>31</sup>	Pakistan	2018	NAFLD	DT	EHR	AUC: 0.73

AUC, area under the curve; CNN, convolutional neural networks; DT, decision tree; EHR, electronic health records; F, fibrosis; ML, machine learning; NLP, natural language processing; NASH, non-alcoholic steatohepatitis; RF, random forest; SVM, support vector machine; XGBoost, eXtreme gradient boosting.



therapeutic strategies. This progression signals a move toward true precision medicine in metabolic liver disease.

### **AI-based diagnostic models using imaging data**

AI technology, especially through ML and deep learning models, is playing a growing role in liver imaging, enhancing the accuracy and speed of disease identification and diagnosis. In clinical evaluation, MASLD imaging typically follows a three-step sequence. Ultrasound serves as the first-line screening tool, with AI assisting in automated detection and grading of steatosis. CT often identifies hepatic fat incidentally during unrelated scans, where AI can quantify fat content retrospectively. MRI then provides confirmation and precise quantification, while AI improves workflow efficiency and interpretive accuracy. In recent years, researchers have developed various quantitative fat analysis methods based on ultrasound, CT, and MRI, enabling clinicians to more accurately assess the degree of hepatic lipid accumulation and fibrosis staging. These methods achieve precise quantification of steatosis and fibrosis by automatically extracting key imaging features, providing critical support for early diagnosis, disease staging, and intervention decision-making.<sup>39</sup>

**Ultrasound imaging:** Ultrasound examination, as a commonly used imaging modality for diagnosing MASLD, is widely applied in clinical practice. Nonetheless, several limitations persist. Diagnostic accuracy still depends on operator expertise and subjective interpretation. Ultrasound, although sensitive for moderate to advanced steatosis, struggles with mild cases. Subtle steatosis remains difficult to detect, as assessments largely rely on qualitative echogenicity rather than quantitative measures.<sup>40</sup> Traditional ultrasound imaging is primarily based on the nonlinear interaction between linearly propagated ultrasonic pulses and tissues, generating harmonic frequencies. Among these, the second harmonic is widely used in clinical image optimization due to its improved signal-to-noise ratio, clear boundaries, and reduced artifacts. However, while qualitative features such as enhanced echoes can be detected when hepatic fat content is elevated, sensitivity remains insufficient for mild fat accumulation. To overcome the limitations of traditional ultrasound, various quantitative ultrasound techniques have been developed in recent years, including elastography, echo signal analysis, and speckle pattern modeling. These methods provide more precise quantitative data on tissue characteristics. For example, ultrasound elastography applies acoustic radiation force pulses via a transducer to measure shear wave velocity within liver tissue, which correlates with tissue stiffness, serving as a non-invasive indicator of fibrosis. Additionally, some algorithms convert the degree of ultrasound attenuation into a controlled attenuation parameter to quantify hepatic fat content. However, these techniques are susceptible to interference from subcutaneous fat thickness and intercostal space width in obese individuals, which can affect the accuracy of the measurements.<sup>41</sup> The integration of AI into ultrasound diagnostics has opened new avenues for MASLD detection. By integrating multiple ultrasound imaging features, AI can more accurately assess liver structure and functional status. In recent years, researchers have conducted several exploratory studies in this field, with relevant findings summarized in Table 2.<sup>42–61</sup> Various research groups have incorporated deep learning, CNN, and large language models to significantly boost the diagnostic accuracy and efficiency of sonographic imaging. Through algorithm optimization and improvements in image processing techniques, AI has enabled quantitative analysis and grading assessment based on traditional ultrasound, thereby providing a more convenient and reliable approach for MASLD screening and classification. A critical

synthesis of recent advancements highlights several distinct, yet complementary, strategies for applying AI to ultrasound-based MASLD diagnosis. These developments move beyond mere automation. They represent a fundamental expansion of ultrasound's diagnostic capability. The first approach centers on improving diagnostic accuracy directly from standard B-mode images. For instance, Kaffas AE *et al.*<sup>42</sup> showed that a deep learning framework could markedly increase both the sensitivity and the accuracy of MASLD diagnosis using routine ultrasound scans. Their findings suggest that AI can uncover subtle imaging cues overlooked in manual interpretation. A second line of work focuses on the automation and standardization of semi-quantitative metrics. This strategy aims to make results more reproducible and less dependent on operator expertise. The AI system developed by the Santoro group illustrates this point well.<sup>43</sup> It automatically calculates the liver-to-kidney ratio, minimizing inter-operator variation and improving consistency across centers. Most notably, a third and transformative direction uses AI to derive quantitative data directly from conventional scans. Models trained on extensive, multi-source datasets that include different scanners and imaging protocols can now estimate liver fat content with high precision. Remarkably, their performance rivals, and in some cases exceeds, that of specialized tools such as FibroScan.<sup>62</sup> Collectively, these studies mark a transformative shift for ultrasound in MASLD. AI is not only augmenting conventional practices but also equipping the modality with novel quantitative capabilities, once exclusive to advanced technologies, thereby significantly boosting its clinical utility.

**CT imaging:** CT remains a widely utilized tool in clinical imaging, offering reliable quantification of liver fat, yet its dependence on manual region-of-interest placement makes the process slow, operator-dependent, and unsuitable for large-scale screening. This inherent limitation has positioned full automation as both the central goal and the main advantage of AI in CT-based MASLD evaluation. Recent research efforts have shifted toward automating CT image analysis using deep learning approaches to facilitate MASLD diagnosis. This technology automatically segments the liver region, identifies features of fat deposition, and subsequently quantifies the degree of hepatic steatosis, thereby providing clinicians with supportive diagnostic information. As summarized in Table 3,<sup>63–71</sup> the research trajectory clearly shows a shift from proof-of-concept automation to validation in large-scale, real-world populations. Following the early validation by Graffy *et al.*,<sup>63</sup> Martín-Saladich *et al.*<sup>64</sup> advanced the field with a fully automated voxel-level framework. Their system achieved excellent cross-device reproducibility and eliminated manual input. The deep learning model aligned closely with manual readings and captured expected associations between steatosis, age, and BMI, reinforcing the biological credibility of AI-derived quantifications. Further refinements have aimed to improve accuracy and integration into clinical workflows. Studies by Prinz *et al.*<sup>65</sup> and Huo *et al.*,<sup>66</sup> both using CNN architectures, reported consistently high agreement between automated and manual fat quantification across multiple metrics. Collectively, the evidence indicates that AI is no longer merely replicating human measurements. It frequently surpasses them in speed, consistency, and spatial coverage, extending analysis from limited region-of-interest samples to whole-liver assessment. In essence, AI-driven automation is transforming CT from a qualitative or semi-quantitative method into a robust, high-throughput platform for MASLD screening and monitoring. By eliminating the bottlenecks of manual analysis, AI unlocks new potential for opportunistic screening within the vast number of CT scans

Table 2. Ultrasound

Author	Country	Year	Categories	Methods	Sample size	Reference standard	Result
Vianna P et al. <sup>44</sup>	Canada	2025	Hepatic steatosis	CNN	250 patients	Nonadapted models	AUC: 0.97
Wu W et al. <sup>45</sup>	China	2025	MASLD	LLM	1,542 participants	CAP	AUC: 0.831
Kaffas AE et al. <sup>42</sup>	USA	2025	Hepatic steatosis	DL	403 patients	MRI-PDFF	AUC: S (0 vs 1/2/3) = 0.813, S (0/1 vs 2/3) = 0.959
Drazinos P et al. <sup>46</sup>	Greece	2025	NAFLD	DL	112 patients	Biopsy	AUC: S (0 vs 1/2/3) = 0.82, S (0/1 vs 2/3) = 0.9156, S (0/1/2 vs 3) = 0.9619
Honarvar M et al. <sup>47</sup>	Canada	2024	MASLD	U-Net architecture	139 subjects	MRI or FibroScan CAP	Sensitivity: 81%, Specificity: 84%
Marques R et al. <sup>48</sup>	Portugal	2024	Hepatic steatosis	Neural network	441 patients; 205 healthy subjects	Ultrasound and elastography	F1 score: ultrasound dataset = 99.5%, elastography dataset = 99.2%, mixed dataset = 98.9%
Liu Y et al. <sup>49</sup>	China	2024	NAFLD	DL	710 individuals	Ultrasound images	AUC: 0.95
Santoro S et al. <sup>43</sup>	Italy	2024	Hepatic steatosis	AI-based algorithm: HRIA	134 patients	MRI-PDFF	AUC: 0.98
Kwon H et al. <sup>50</sup>	Korea	2024	NAFLD	AI-QUS	35 participants	MRI-PDFF	AUC: S (0 vs 1/2/3) = 0.93, S (0/1 vs 2/3) = 0.99, S (0/1/2 vs 3) = 0.98
Vianna P et al. <sup>51</sup>	Canada	2023	Hepatic steatosis	DL	199 patients	Biopsy	AUC: S (0 vs 1/2/3) = 0.85, S (0/1 vs 2/3) = 0.73, S (0/1/2 vs 3) = 0.67
Yang Y et al. <sup>52</sup>	China	2023	NAFLD	DL	928 participants	Abdominal ultrasound	AUC: 0.90
Jeon SK et al. <sup>53</sup>	Korea	2023	NAFLD	CNN	173 participants	MRI PDFF	AUC: 0.97
Zsombor Z et al. <sup>54</sup>	Hungary	2023	NAFLD	AI-calculated hepatorenal index (AI-HRI)	102 patients	MRI-PDFF	AUC: Mild steatosis = 0.758, Moderate/severe steatosis = 0.803
Li B et al. <sup>55</sup>	USA et al.	2022	NAFLD	DL	3,310 patients	Histology	AUC: Mild steatosis = 0.85, Moderate steatosis = 0.91, Severe steatosis = 0.93
Byra M et al. <sup>56</sup>	USA	2022	NAFLD	CNN	135 participants	MRI-PDFF	AUC: PDFF $\geq$ 5% = 0.91, PDFF $\geq$ 10% = 0.86
Che H et al. <sup>57</sup>	USA	2021	NAFLD	CNN	55 subjects	Biopsy	AUC: 0.978
Constantinescu EC et al. <sup>58</sup>	Romania	2021	NAFLD	CNN	629 grayscale liver images	B-mode ultrasound and elastography	AUC: 0.93
Han A et al. <sup>59</sup>	Poland	2020	NAFLD	CNN	204 participants	MRI-PDFF	AUC: 0.98
Cao W et al. <sup>60</sup>	China	2020	NAFLD	DL	240 participants	Abdominal ultrasound	AUC: 0.933
Byra M et al. <sup>61</sup>	Poland	2018	Hepatic steatosis	CNN, SVM	55 severely obese patients	Liver biopsy	AUC: 0.977

AUC, area under the curve; AI, artificial intelligence; AI-QUS, artificial intelligence-enhanced quantitative ultrasound; CNN, convolutional neural networks; DL, deep learning; LLM, large language models; S, steatosis grades; SVM, support vector machine.

**Table 3. CT**

Author	Country	Year	Categories	Methods	Sample size	Reference standard	Result
Kim HY <i>et al.</i> <sup>67</sup>	Korea	2025	Hepatic steatosis	DL	3,620 subjects	Liver biopsy	AUC: 0.868
Vong T <i>et al.</i> <sup>68</sup>	USA	2025	Hepatic steatosis	LLM	200 adults	Labeled CT reports	Accuracy: 0.988, Sensitivity: 0.98, Specificity: 1
Martín-Saladich Q <i>et al.</i> <sup>64</sup>	Spain	2024	MAFLD	nn-UNet	39 patients	Manually assessed by specialists	AUC: 0.94
Yoo J <i>et al.</i> <sup>69</sup>	Korea	2024	Hepatic steatosis	DL	362 adults	MRS-PDFF	AUC: 0.817
Jeon SK <i>et al.</i> <sup>70</sup>	Korea	2024	Hepatic steatosis	DL	252 participants	MRS-PDFF	AUC: 0.806
Prinz S <i>et al.</i> <sup>65</sup>	Germany	2023	Hepatic steatosis	CNN	197 patients	Manual ROIs	0.75<AUC<0.87
Pickhardt PJ <i>et al.</i> <sup>71</sup>	USA <i>et al.</i>	2021	Hepatic steatosis	DL	1,204 healthy adults	Unenhanced CT	AUC: PDFF ≥ 5% = 0.669, PDFF ≥ 10% = 0.854
Graffy PM <i>et al.</i> <sup>63</sup>	Madison	2019	NAFLD	DL	9,552 adults	The manual Hounsfield unit measures	R <sup>2</sup> : 0.92
Huo Y <i>et al.</i> <sup>66</sup>	USA	2019	NAFLD	CNN	246 subjects	Abdominal CT scans with manual liver segmentation	Pearson correlations = 0.94

CT, computed tomography; AUC, area under the curve; CNN, convolutional neural networks; DL, deep learning; LLM, large language models; nn-UNet, neural network-UNet; R<sup>2</sup>, coefficient of determination; ROI, region of interest.

acquired for unrelated reasons. This shift adds significant value to everyday imaging practice and paves the way for population-level steatosis surveillance.

**MRI imaging:** MRI, as a non-invasive technique for hepatic fat quantification, has been widely used in both research and clinical practice. Common MRI-based fat quantification methods include magnetic resonance spectroscopy (MRS), fat-suppressed imaging, water-fat separation techniques, and proton density fat fraction (PDFF). Among these, MRS is considered one of the most precise for non-invasively quantifying intrahepatic fat. It can sensitively detect metabolic changes and pathophysiological states in living tissue and has advantages such as low measurement variability, high correlation with histology, and results that are not affected by liver fibrosis, iron deposition, or dietary factors.<sup>72</sup> However, a limitation of MRS is that it can only quantify fat content in a single localized region, making it difficult to comprehensively assess fat distribution throughout the entire liver. In contrast, the PDFF technology can reflect the fat content of the entire organ. After multi-factor correction, its quantitative accuracy is highly consistent with MRS and is regarded as a dependable indicator for assessing steatosis. Both MRI-PDFF and MRS have demonstrated strong concordance with histopathological steatosis grading and offer high diagnostic accuracy for the clinical classification of hepatic fat content.<sup>73,74</sup> Rather than revalidating MRI-based fat quantification—which is already well established—current research focuses on workflow optimization, computational efficiency, and improved clinical accessibility. As outlined in Table 4,<sup>74–81</sup> recent deep learning advances are systematically resolving major limitations in MRI analysis. A leading direction involves automating labor-intensive steps. Martí-Aguado *et al.*<sup>75</sup> developed a CNN algorithm for automated whole-liver segmentation, achieving fat quantification results with strong histological concordance. Another stream of innovation targets refinement of the PDFF metric through advanced neu-

ral networks. With the advancement of AI technology, performance evaluation of metrics such as PDFF has also been optimized. Wang *et al.*<sup>76</sup> used deep learning to infer PDFF values with high precision, reinforcing its reliability as an imaging biomarker. Meneses *et al.*<sup>77</sup> proposed the Variable Echo Times Neural Network, which delivered more accurate PDFF estimation than conventional architectures. Despite these technical gains, clinical translation of MRI-PDFF and MRS remains constrained by high cost, specialized hardware, and long acquisition times. Consequently, these modalities are mostly applied in research contexts or for evaluating high-risk patients rather than general screening. Thus, although AI has greatly advanced the precision, automation, and interpretability of MRI-based fat quantification, these methods remain endpoints within the diagnostic pathway, not tools for population-level screening.

**AI-based analytical models for liver histopathology**

Liver biopsy continues to serve as the diagnostic gold standard for MASLD. However, its invasiveness, sampling error, and subjective scoring limit its routine use. In response, AI and digital pathology are redefining histological assessment, offering objective, reproducible, and scalable tissue evaluation. New algorithms can now automatically detect and quantify key histological features from biopsy samples, such as fat accumulation, lobular inflammation, ballooning degeneration, and fibrosis. The results demonstrate high concordance with assessments made by experienced pathologists. A critical review of ongoing research reveals a multi-faceted evolution in AI-assisted liver pathology. This shift is not simply incremental—it reflects a conceptual reorientation toward algorithm-supported diagnostics. AI-driven image analysis systems can perform precise evaluations of digitized histological slides, automatically identifying core pathological changes associated with MASLD. Among these, hepatocyte ballooning is a key morphological marker for diagnosing MASLD. The ad-

Table 4. MRI

Author	Country	Year	Catego- ries	Meth- ods	Sample size	Reference standard	Result
Meneses JP <i>et al.</i> <sup>77</sup>	Chile	2025	Hepatic steatosis	VET-Net	188 subjects	MRI-PDFF	$R^2$ : 0.87–0.98
Li S <i>et al.</i> <sup>78</sup>	China	2024	NAFLD	DL	20 subjects	Graph-cut algorithm	No significant difference
Wang K <i>et al.</i> <sup>76</sup>	USA	2023	NAFLD	CNN	292 participants	CSE-MRI	CNN-inferred PDFF showed superior agreement with reference (ICC = 0.99, bias = –0.19%)
Bastati N <i>et al.</i> <sup>79</sup>	Austria	2023	NAFLD	UDC	46 patients	Histology	AUC: 0.85
Kim JW <i>et al.</i> <sup>74</sup>	Korea	2022	NAFLD	MRS, MRI-PDFF	47 patients	Biopsy	AUC: $\geq S2$ (MRS) = 0.860, (MRI-PDFF) = 0.846, $\geq S3$ (MRS) = 0.878, (MRI-PDFF) = 0.855
Martí-Aguado D <i>et al.</i> <sup>75</sup>	Spain	2022	NAFLD	DL	165 participants	Biopsy	AUC: 0.97
Pollack BL <i>et al.</i> <sup>80</sup>	Pittsburgh	2021	NAFLD	CNN	149 patients	Biopsy	AUC: 0.84
Cho Y <i>et al.</i> <sup>81</sup>	Korea	2021	NAFLD	DL	77 samples	Manual Segmentation	Step 3: Dice Coefficients $0.94 \pm 0.01$ , Bland-Altman bias –0.67%

MRI, magnetic resonance imaging; AUC, area under the curve; CNN, convolutional neural networks; DL, deep learning; UDC, unsupervised deep clustering; VET-Net, variable echo times neural network; ICC, intraclass correlation coefficient;  $R^2$ , coefficient of determination; ROI, regions of interest; S, steatosis grades; WLS, whole-liver segmentation.

vancement of digital pathology helps overcome limitations of traditional manual slide reading, such as low annotation efficiency and high subjective variability, by enhancing diagnostic objectivity and consistency through high-resolution image acquisition and algorithmic analysis. The combination of high-resolution slide digitization with algorithmic analysis enhances diagnostic precision and facilitates standardization across centers. Yet, methodological gaps persist. The scarcity of large, annotated, and diverse datasets limits generalizability, especially across staining methods, scanners, and populations. Future research urgently needs to construct a large-scale, standardized image database of ballooning degeneration in liver cells and further optimize algorithm structures (such as introducing the Transformer architecture) to improve recognition accuracy. As generative AI continues to mature, the establishment of standardized performance criteria will be crucial for validating its role in augmenting diagnostic consistency.<sup>82</sup> Traditional ML models typically depend on extensive labeled datasets to reach high precision, and their deployment in clinical practice is often hampered by concerns over patient privacy and data sensitivity. To this end, the emerging quantum machine learning (QML), as an interdisciplinary technology that fuses quantum computing and classical ML, shows stronger generalization ability and modeling accuracy. Lusnig *et al.*<sup>83</sup> demonstrated the potential of hybrid quantum-classical neural networks, achieving 97% accuracy in classifying biopsy slides. This approach performed particularly well under data-limited conditions, suggesting that QML may address two persistent challenges: the need for extensive annotation and the protection of data privacy. Beyond static diagnosis, AI is now enabling dynamic disease monitoring. Naoumov *et al.*<sup>84</sup> integrated AI with digital pathology to track histological changes during MASH therapy. Their system provided greater sensitivity in detecting fibrosis regression and enabled more dynamic evaluation of therapeutic efficacy. Together, these advances represent more than automation. They signal a paradigm shift—from

subjective interpretation toward reproducible, data-driven quantification—reshaping the epistemological foundation of liver pathology itself.

### Treatment of MASLD

The treatment of MASLD primarily includes lifestyle modification and pharmacotherapy (Table 5).<sup>85–94</sup> The convergence of AI and smart devices is reshaping these traditional strategies, promoting a shift from standardized care to dynamic, personalized, and data-driven management. In lifestyle management, patients are advised to control weight, limit alcohol intake, improve dietary structure, and adhere to regular exercise. In terms of drug therapy, several drug candidates are currently in clinical trials. In addition, patients with chronic hepatitis B who have concomitant metabolic abnormalities (such as glucose dysregulation, dyslipidemia, or overweight) should also be comprehensively evaluated and actively intervene with their metabolic markers to reduce the risk of MASLD progression. Probiotic therapy has also been recognized as potentially valuable in the management of MASLD. It has been shown that probiotics can play a positive role in improving liver enzyme levels, regulating lipid metabolism, promoting weight control, and alleviating insulin resistance by modulating intestinal flora.<sup>95</sup> Bariatric surgery has emerged as an alternative treatment option for patients with MASLD combined with obesity who do not respond well to lifestyle interventions and medications. Chen S *et al.*<sup>96</sup> used a multi-omics approach to analyze the support for the use of sleeve gastrectomy as an effective means of ameliorating hepatic steatosis and inflammation when other weight loss strategies are ineffective.

### Lifestyle interventions

Lifestyle-related factors play a pivotal role in the onset and progression of MASLD. Yuan *et al.*<sup>97</sup> demonstrated that in-



**Table 5. Treatment**

Author	Country	Year	Cat-egories	Drugs	Methods	Reference	Result
Harrison SA <i>et al.</i> <sup>90</sup>	USA	2025	MASH	FFAR1/FFAR4 agonist	RCT	Placebo	Response rates: 300 mg = 29.3%, placebo = 11.3%
Ozlu Karahan T <i>et al.</i> <sup>91</sup>	Turkey	2025	MASLD	NA	LLM	Guidelines	Accuracy: mean energy = 91.3 ± 11.0%
Zhang L <i>et al.</i> <sup>88</sup>	China	2025	MAFLD	Qigui Jiangzhi Formula (QGJZF)	AlphaFold-AI	pTM scores (range 0–1)	pTM scores: PRKAA2 = 0.97, SIRT1 = 0.93
Harrison SA <i>et al.</i> <sup>85</sup>	UK	2024	NASH	Resmetirom	RCT	Placebo	NASH resolution rate: 100 mg = 29.9%, placebo = 9.7%
Wang Y <i>et al.</i> <sup>87</sup>	China	2024	NASH	LiDi FGF21	LiDi platform	Baseline	NAS scores: low-dose = 3.83 ± 0.98, high-dose = 3.33 ± 0.82, baseline = 6.00 ± 0.63
Newsome PN <i>et al.</i> <sup>92</sup>	UK <i>et al.</i>	2023	NASH	AOC3 inhibitor	Double-blind, placebo-controlled	Placebo	AOC3 activity relative to baseline: 10 mg = 3.3%, Placebo = 90.4%
Saldarriaga OA <i>et al.</i> <sup>89</sup>	USA	2023	MASLD	NA	DL	Key Findings	Upregulated Targets: CCR2, CCR5, CCL2, CCL5, LGALS3
Yu H <i>et al.</i> <sup>93</sup>	China	2023	NAFLD	Aescin (Aes)	HepG2 cell models	/	Aes facilitates Nrf2 nuclear translocation
Sessa L <i>et al.</i> <sup>86</sup>	Italy <i>et al.</i>	2023	NASH	5-hydroxytryptamine 2A receptor (5-HT2AR)	SoftMining Platform	5HT2AR-CHO-K1 cells	Competitive binding studies in 5HT2AR-CHO-K1 cells validated the <i>in silico</i> prediction
Lee WY <i>et al.</i> <sup>94</sup>	Korea	2022	NAFLD	Flavonoids	Machine-learning model: AI-DTI	HepG2/AML12 cell models	Screening and functional validation of candidate flavonoids

ALT, alanine aminotransferase; AOC3, amine oxidase copper-containing 3; DL, deep learning; LiDi, lipidation-dimerization; LLM, large language models; NASH, non-alcoholic steatohepatitis; RCT, randomized controlled trial; pTM, predicted tem plate modeling; NAS scores, nonalcoholic fatty liver disease activity score.

tensive lifestyle intervention can reverse hepatic fibrosis in MASH, with AI-assisted imaging revealing the most evident regression in the portal region. However, maintaining adherence to such interventions remains difficult—particularly among socioeconomically disadvantaged groups, who often face higher MASLD risk due to poor dietary habits.<sup>98</sup> AI-enabled smart devices provide scalable and individualized solutions for this challenge.

In recent years, with the help of smart devices combined with AI algorithms, clinicians can achieve real-time monitoring of patients' diet, physical activity, and metabolism-related indicators, and then generate personalized intervention programs. For example, a model based on Gradient Boosting Regression predicts individual postprandial glucose fluctuations and combines gut microbiome data with dietary habits to optimize an individualized dietary structure.<sup>99</sup> They are especially valuable for patients with prediabetes or type 2 diabetes and MASLD, where precise glycemic control is essential.

Nutritional strategies are fundamental in the prevention and management of MASLD. Among various dietary patterns, the Mediterranean diet has shown considerable efficacy in lowering hepatic lipid accumulation and improving metabolic health.<sup>100</sup> With the support of smart devices and AI, the implementation of medical nutrition therapy is more

efficient and precise. Patients can use the image recognition feature to record their daily diet. The system automatically analyzes the nutritional content and guides them to follow a healthy diet structure while dynamically adjusting energy intake based on real-time data. It has been demonstrated that this type of intelligent system is effective in improving liver triglyceride levels and other metabolic parameters.<sup>101</sup> This scenario suits motivated individuals who benefit from structured, feedback-driven dietary support.

With advancements in digital health, smart devices now offer capabilities such as remote patient monitoring and on-line follow-up, allowing healthcare providers to track real-time fluctuations in liver-related biomarkers—including alanine aminotransferase and aspartate transaminase—as well as body weight. This continuous monitoring facilitates timely treatment adjustments based on a patient's clinical progression. This is equally useful for patients undergoing new drug therapies or those with advanced fibrosis who require close follow-up.

AI chatbots are also gradually playing a role in assisted management, providing not only medication reminders and health education but also basic psychological support that can help improve patient compliance. Related studies show that some AI chatbots currently score high on health-related questions, but clinical application still requires professional

medical judgment. With continued algorithm optimization, their clinical practicality is expected to improve further in the future.<sup>102</sup> In overburdened healthcare systems, AI chatbots and digital companions can also serve as first-line educational tools, addressing common patient concerns and reinforcing adherence.

AI-powered systems further support individualized care by integrating clinical data, laboratory results, and histopathological findings to formulate tailored therapeutic plans that span lifestyle modifications and pharmacologic options. Mobile health applications and wearable devices are becoming increasingly valuable tools in MASLD care. These tools enable the ongoing collection of behavioral data, including physical activity, dietary intake, and sleep metrics, which supports more precise and dynamic intervention strategies.<sup>103</sup> Exercise is another widely accepted intervention with proven benefits for MASLD. Regular physical activity not only contributes to weight reduction and decreased hepatic fat but also elevates high-density lipoprotein cholesterol levels.<sup>104</sup> A health management app that combines AI algorithms can help patients set personalized exercise plans and dynamically adjust them based on feedback from wearable sensors. At the same time, these devices can also monitor indicators such as weight and waist circumference in real time and work with AI models to predict the potential effects of weight loss on liver fat improvement. Studies have shown that achieving a weight loss of over 10% can result in substantial improvements in MASH and liver fibrosis severity.<sup>105</sup> Closed-loop feedback mechanisms enhance motivation, especially for individuals struggling with weight maintenance, by offering concrete targets and continuous reinforcement.

### Drug development

While pharmacological research into MASLD therapies has advanced in recent years, only a limited number of medications have received approval. Drugs currently in late-stage clinical development include incretin-based therapies like glucagon-like peptide-1 and its multi-agonists, metabolic modulators like peroxisome proliferator-activated receptor, fibroblast growth factor 21 (FGF21), and thyroid hormone receptor  $\beta$  (THR- $\beta$ ) agonists, or novel drugs targeting new mechanisms, such as fatty acid synthase inhibitors.<sup>106,107</sup> The development of AI technology has significantly accelerated the research and development process of MASLD-related drugs in multiple stages. Through virtual screening, structural prediction, and multi-omics integration analysis, AI has not only promoted new drug discovery but also driven the re-development of existing drugs for new indications. For example, Resmetirom is a highly selective THR- $\beta$  agonist. A notable breakthrough occurred in 2024 when the U.S. Food and Drug Administration approved Resmetirom as the first drug for treating MASH. AI-assisted analysis was extensively used in the target identification, mechanism elucidation, and clinical study design of this drug. In its pivotal Phase III clinical trial, AI algorithms were used to quantitatively assess changes in liver fibrosis before and after treatment, demonstrating that Resmetirom has definitive efficacy in significantly improving liver fibrosis.<sup>85,108,109</sup> In addition, the potential of AI in drug screening and indication expansion continues to be validated. HuX *et al.* utilized the DiscoveryStudio19 platform, which integrates virtual screening, molecular docking, ADME property prediction, and toxicity assessment, to screen potential farnesoid X receptor agonists, providing a new drug candidate idea for MASH treatment.<sup>110</sup> Similarly, Sessa L and colleagues leveraged AI methodologies to validate the therapeutic potential of the 5-hydroxytryptamine 2A receptor,

identifying its antagonists as promising candidates for MASH therapy.<sup>86</sup> In the field of protein therapy research, Wang Y's team has developed a new form of bioactive FGF21 based on the "lipidation-dimerization" platform, named LiDi FGF21. This molecule demonstrates superior pharmacological properties, expanding the application prospects of protein-based drugs in the treatment of MASLD.<sup>87</sup> AI technology also provides new insights into the modernization of traditional Chinese medicine. Zhang L *et al.* identified potential target proteins for the traditional Chinese medicine compound QGJZF in MASLD using the SymMap database and predicted the structures of its key proteins using AlphaFold, revealing that it may exert anti-adipogenic and anti-inflammatory effects through the AMPK/SIRT1-TFEB pathway.<sup>88</sup> Furthermore, Saldaña *et al.* applied deep learning to multi-dimensional datasets in fatty liver fibrosis, identifying disease-stage-dependent heterogeneity in macrophage populations and highlighting CCR2 and Galectin-3 as potential therapeutic targets in advanced MASLD.<sup>89</sup>

In summary, AI is fundamentally reshaping MASLD drug discovery by accelerating target identification, optimizing clinical trials, and enhancing predictive profiling.<sup>111</sup>

### Ethical, regulatory, and data security considerations

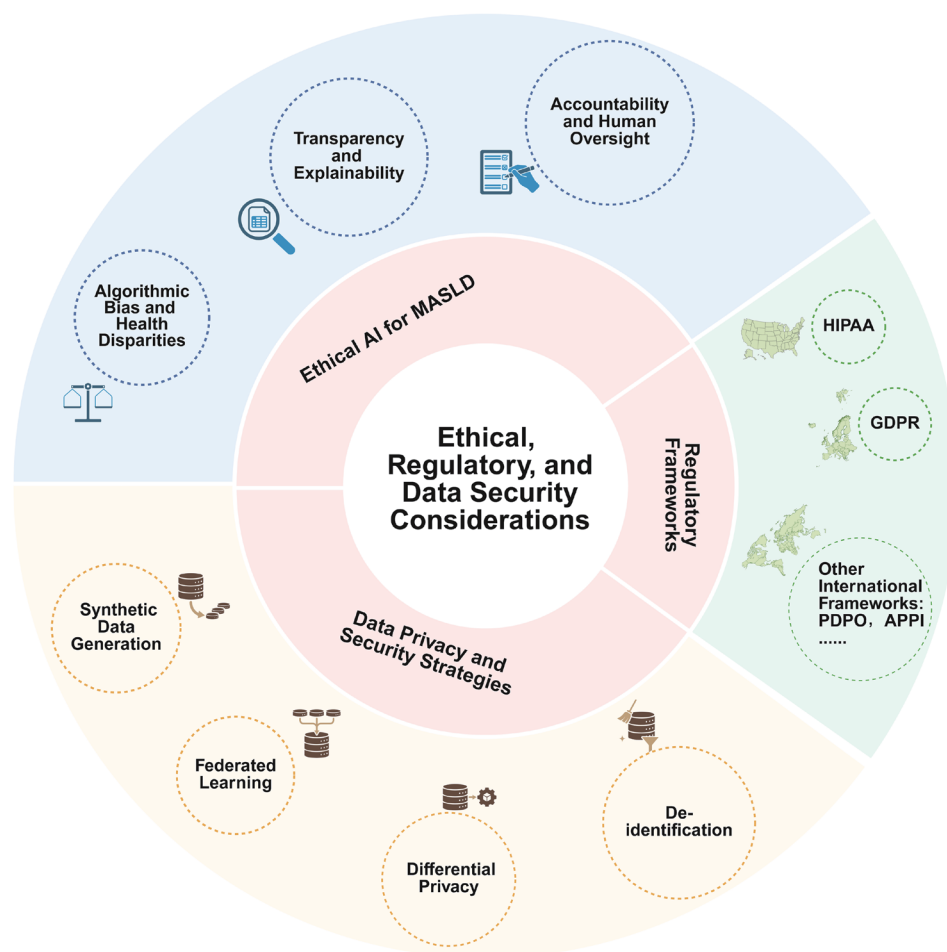
Integrating AI and smart devices into MASLD care thus holds great promise for improving diagnostic precision and therapeutic outcomes.<sup>112</sup> However, its real-world application raises complex ethical, regulatory, and data security concerns (Fig. 3). Therefore, the development and deployment of AI must align with ethically grounded frameworks, consistent with the World Health Organization guidance on the Ethics and Governance of AI for Health. The World Health Organization identifies six guiding principles: protecting autonomy; advancing human welfare and safety; ensuring transparency and intelligibility; reinforcing accountability; promoting equity and inclusiveness; and encouraging responsiveness and sustainability.<sup>113</sup>

Recent analyses reveal that bias and fairness dominate ethical discourse, followed by concerns about safety, reliability, transparency, accountability, model misuse, and privacy—particularly in relation to large language models.<sup>114,115</sup> Concurrently, the evolution of AI operates within established regulatory structures, which define critical operational boundaries and reinforce the protection of personal data and privacy.<sup>116</sup> As jurisdictions adapt their own legal standards, an international consensus toward harmonized regulation is increasingly essential.

From a technical standpoint, privacy-preserving techniques, such as federated learning and differential privacy, are vital to building multi-layered safeguards. Only through such a multidisciplinary approach can these innovative tools be deployed safely and equitably, upholding the rights and welfare of individuals in real-world settings.

### Ethical AI for MASLD

**Algorithmic bias and health disparities:** The performance and generalizability of AI models depend critically on the diversity of their training data. When development datasets are disproportionately sourced from limited demographic segments, such as particular ethnic, geographic, or socioeconomic groups, models are prone to substantial performance decline in clinically underrepresented populations. This not only reduces clinical reliability but may also amplify existing health inequities.<sup>117</sup> To mitigate such effects, it is essential to systematically construct diverse and inclusive training cohorts and incorporate bias detection and mitiga-



**Fig. 3. Responsible Artificial intelligence in metabolic dysfunction-associated steatotic liver disease: A framework built on ethics, regulation, and security.** (Created in BioRender). AI, artificial intelligence; MASLD, metabolic dysfunction-associated steatotic liver disease; HIPAA, health insurance portability and accountability act; GDPR, general data protection regulation; PDPO, personal data (privacy) ordinance; APPI, act on the protection of personal information.

tion protocols across the entire model lifecycle. These strategies should consider local context—target demographics, deployment settings, algorithm type, and the specific biases being addressed.<sup>118</sup>

**Transparency and explainability:** Many advanced AI systems, particularly deep learning-based systems, function as “black boxes” due to their inherently opaque internal decision logic, which remains largely inaccessible to human interpretation. For healthcare providers to trust AI-based diagnostic aids, such as hepatic steatosis grading, transparency in algorithmic reasoning is essential.<sup>119</sup> Explainable AI (XAI) addresses this need by employing both global and local interpretability techniques to uncover salient features contributing to predictive outcomes. This capacity to elucidate model behavior is critical for fostering informed clinical acceptance and enabling the responsible embedding of AI tools into medical practice.<sup>120</sup>

**Accountability and human oversight:** Excessive dependence on AI in medical contexts can lead to significant errors in areas such as predictive analytics, system oversight, device selection, and even clinical decision-making. Many AI models are often inadequately trained on specific features, such as dialects and medical colloquialisms; they risk generating inaccurate diagnoses, medication explana-

tions, or treatment recommendations.<sup>121</sup> It is therefore essential to reaffirm that AI serves strictly as an adjunctive decision-support mechanism rather than as an autonomous clinical authority. The final judgment and accountability for all diagnostic or therapeutic decisions must rest with qualified healthcare professionals. These practitioners must critically appraise algorithm-generated suggestions and retain the ultimate decision-making power, ensuring consistent human oversight and intervention throughout patient care.

### Regulatory frameworks

The development and deployment of medical AI must occur within a robust regulatory framework, with the core objective of safeguarding patient data privacy and security. Several major frameworks currently provide guidance for this evolving landscape.

**Health Insurance Portability and Accountability Act (HIPAA):** In the United States, HIPAA stands as a foundational statute safeguarding Protected Health Information.<sup>122</sup> Despite its importance, HIPAA's jurisdiction is incomplete—it excludes data handled by non-covered entities, omits patient-generated content, and overlooks extensive non-health datasets that can indirectly reveal health conditions. To establish comprehensive protection for the health information

ecosystem, it is imperative to either expand HIPAA's applicability or create a separate regulatory regime for currently uncovered health-related data. Proposed legislative pathways include enacting a general health data protection rule supplemented by specific provisions for different data processors, or adopting a unified framework inspired by the EU's General Data Protection Regulation (GDPR) that applies to all personal data processors while incorporating dedicated rules for health information.<sup>123</sup>

**GDPR:** The European Union's GDPR regulation has become a global benchmark for personal data governance.<sup>124</sup> It mandates strict adherence to the principles of lawfulness, fairness, and transparency in all stages of data processing. Under GDPR, information must be collected for clearly defined and legitimate purposes (purpose limitation), and only the minimal data necessary for those purposes may be processed (data minimization). Controllers remain fully accountable for compliance with these standards. In MASLD-related studies involving EU participants, explicit informed consent and transparent data handling practices are indispensable, reflecting the regulation's emphasis on autonomy and accountability.

**Other international frameworks:** Comparable data protection systems have been enacted in multiple jurisdictions. Prominent examples encompass the Personal Data (Privacy) Ordinance (PDPO) in Hong Kong, China<sup>125</sup> and Japan's Act on the Protection of Personal Information (APPI).<sup>126</sup> Both are grounded in the shared values of purpose limitation, proportionality, and accountability, offering principled oversight of personal data processing.

Nevertheless, legal compliance alone does not guarantee full protection.<sup>127,128</sup> It underscores the necessity for multi-layered privacy-preserving architectures in AI-driven MASLD research.

### **Data privacy and security strategies**

To navigate these complex regulatory terrains and mitigate privacy risks, advanced technical safeguards have been progressively incorporated into AI systems.<sup>129</sup>

**De-identification:** De-identification aims to remove or obscure personal identifiers from data. In structured data, methods such as polymorphic encryption have improved resilience against re-identification while maintaining analytical utility. Moreover, large language models are now capable of achieving higher accuracy in automatic de-identification of unstructured text, substantially improving privacy protection for clinical narratives.<sup>130</sup>

**Differential privacy:** Differential privacy introduces calibrated random noise into datasets or query results, thereby ensuring that the inclusion or exclusion of any single individual cannot be inferred.<sup>131</sup> This approach ensures that the presence or absence of any individual in the dataset cannot be inferred from the analysis results, while still preserving the accuracy of statistical findings at the aggregate level.

**Federated learning:** Federated learning enables distributed model training across multiple institutions without the exchange of raw data. This paradigm is particularly advantageous for multicenter MASLD studies, allowing algorithmic generalization and cross-population robustness while keeping sensitive data localized within each contributing hospital or research site.<sup>132</sup>

**Synthetic data generation:** Synthetic data technology creates artificial datasets that mimic the statistical properties of real-world data but exclude actual patient information.<sup>133</sup> Such datasets can be used safely for model testing and algorithm refinement, effectively eliminating privacy concerns inherent in traditional EHR-based development.

### **Clinical translation of AI in MASLD: Beneficial populations, clinical scenarios, and future pathways**

This section explores the transition of AI from research prototypes to real-world applications in MASLD management. It identifies the clinicians and patient populations most likely to benefit and highlights key clinical scenarios where these tools add measurable value. Within this framework, AI emerges not merely as a computational instrument but as a strategic enabler of precision medicine and more equitable healthcare delivery.<sup>134</sup>

#### **Populations that would benefit most**

AI technologies hold considerable promise for improving MASLD management—enhancing diagnostic accuracy, facilitating early intervention, and widening access to care, especially in resource-limited settings.<sup>135</sup> They also contribute to objective evaluation metrics in clinical research and therapeutic trials.

**Healthcare professionals:** For physicians in hepatology, radiology, or primary care, AI-based decision support offers substantial gains. By reducing observer variability and highlighting subtle imaging features, such systems improve diagnostic confidence and consistency. They can also automate repetitive workflows—such as steatosis quantification—and prioritize high-risk cases. For junior clinicians or those outside tertiary centers, these tools function as valuable learning aids and clinical references.<sup>136</sup>

**Populations in resource-limited settings:** In underserved areas lacking hepatology expertise, AI-enabled portable ultrasound and automated image analysis can decentralize screening from hospitals to communities. This decentralization promotes earlier diagnosis and intervention. Moreover, digital platforms powered by AI can facilitate remote counseling and adherence tracking, helping sustain long-term care continuity.<sup>137</sup>

**High-risk populations for primary prevention:** Individuals with obesity, type 2 diabetes, metabolic syndrome, or related cardiometabolic risk factors form a critical group for preventive strategies. AI-based prediction models integrating routine laboratory and clinical data can identify early hepatic involvement, offering a valuable window for timely lifestyle or pharmacologic intervention before irreversible fibrosis develops.<sup>138</sup>

**Patients enrolled in clinical trials or on pharmacotherapy:** In advanced clinical settings, AI-driven digital pathology and imaging analytics provide reproducible quantification of histologic changes, such as steatosis reduction or fibrosis regression.<sup>139</sup> These capabilities enhance precision in endpoint measurement, optimize trial efficiency, and support data-driven therapeutic adjustments.

#### **Clinical scenarios of application**

AI integration benefits several key clinical workflows, from early detection to long-term management.

**Risk stratification and routine screening:** When embedded in primary care systems, AI algorithms analyzing EHR and imaging data can flag individuals at risk of MASLD.<sup>140</sup> This shift toward proactive, data-informed screening represents a major step away from reactive treatment models.

**Lifestyle management and adherence promotion:** Mobile health tools and smart wearables can monitor diet, exercise, and metabolic indicators in real time.<sup>141</sup> Their feedback mechanisms encourage behavioral adherence and enable personalized guidance through clinician-patient connectivity.

**Disease monitoring and follow-up:** Remote AI sys-



tems leveraging wearable sensors allow continuous disease tracking beyond clinical visits. They can detect early warning signs of progression or noncompliance, reducing reliance on in-person follow-up and improving care accessibility for rural populations.<sup>142</sup>

**Drug response monitoring in drug development:** In drug trials, AI-enhanced imaging (such as MRI-PDFF) and computational pathology provide precise, objective measures of treatment efficacy, such as improvements in fibrosis stage or reductions in steatosis burden.<sup>143,144</sup> These methods streamline endpoint evaluation, improving the efficiency and robustness of MASLD drug development.

### **Strengths, challenges, and future research directions**

AI is increasingly recognized as a transformative force in healthcare, offering substantial opportunities to enhance diagnostic accuracy and clinical decision-making. However, realizing its full potential in MASLD management requires overcoming substantial technical, ethical, and translational challenges through continuous research and validation.

**Strengths: Expanding diagnostic and clinical utility:** Evidence increasingly supports the value of AI in refining diagnostic accuracy for hepatic steatosis and fibrosis while reducing interobserver variability. Beyond diagnostics, integration with wearable and behavioral data enables personalized interventions, sustained adherence, and dynamic disease tracking. Continuous monitoring of behavioral, metabolic, and lifestyle parameters enables tailored recommendations—ranging from dietary guidance to activity adjustment—while reinforcing patient adherence. Parallel progress in AI-driven drug discovery and trial optimization further accelerates the identification of novel therapeutic targets and the objective evaluation of drug efficacy. Collectively, these advances expand the reach of precision hepatology and strengthen data-driven care.

**Challenges and clinical translation limitations:** Despite this progress, routine clinical adoption remains limited. Most AI models rely on retrospective, single-center data, constraining generalizability. Moreover, reference standards differ widely—ranging from histology to MRI or controlled attenuation parameter—hindering comparison. The opaque “black-box” characteristics of many deep learning systems also impede clinician trust and limit regulatory approval. Equally pressing are the gaps in study populations and outcomes. Patients with viral hepatitis, alcohol-related liver disease, or mixed etiologies are frequently underrepresented, and few studies provide robust longitudinal or cost-effectiveness data. Beyond technical challenges, systemic and social barriers also persist. Cost barriers, inadequate digital literacy, and uneven device access exacerbate disparities, especially across rural or low-income communities. Even where devices are available, age, education, and cultural norms may limit engagement. Advanced imaging technologies such as MRI, though powerful, remain concentrated in tertiary centers and entail high costs, reinforcing inequity. Without targeted digital inclusion strategies, these innovations risk amplifying rather than reducing healthcare inequity.

### **Future research directions**

Bridging the divide between laboratory innovation and real-world application is now a central goal for AI in MASLD. Future research must target current gaps—limited external validation, inadequate multimodal integration, and scarce real-world evidence—through a deliberate and iterative translational framework.

First, algorithmic innovation and data fusion are essential. The next generation of models should be interpretable, resilient, and computationally efficient, capable of integrating imaging, clinical, biochemical, and behavioral data. Techniques such as foundation models, transfer learning, and even QML may offer pathways to improved adaptability, particularly in low-data or resource-constrained settings.

Second, systematic validation and consensus-building must follow. Large-scale, multicenter cohorts across diverse populations are vital to ensure external robustness. Standardized annotation protocols, harmonized evaluation metrics, and shared reference datasets would further support reproducibility and comparability across platforms.

Third, ethical and regulatory translation must advance in parallel with technological progress. XAI and privacy-preserving strategies such as federated learning can strengthen transparency and data security, fostering clinical and regulatory acceptance.

Finally, real-world implementation should become an integral part of future studies. Pilot deployments within clinical environments, supported by adaptive policy frameworks, can evaluate usability, workflow compatibility, and economic impact. Continuous learning systems that incorporate patient-generated data and digital biomarkers can, in turn, support dynamic, personalized management. Collectively, these coordinated efforts provide a pragmatic roadmap for transforming AI-driven MASLD research into tangible clinical benefit.

### **Conclusions**

The integration of AI and smart devices is progressively reshaping the comprehensive management framework for MASLD, offering novel perspectives on improving clinical outcomes. By harnessing diverse datasets, including EHR and imaging studies, AI-based predictive tools have greatly enhanced early disease detection, particularly in primary care and for identifying at-risk individuals before symptom onset. In the field of imaging diagnosis, AI-based quantitative analysis technologies for ultrasound, CT, and MRI have effectively overcome the limitations of traditional methods in terms of sensitivity and subjectivity, making reliable assessment more accessible in non-specialist settings. Beyond standard imaging modalities, AI’s analytical power is also being applied to digital pathology. Emerging algorithms, such as QML, have demonstrated high accuracy in liver pathology image recognition, opening up new avenues for non-invasive diagnostic methods. Meanwhile, wearable devices allow real-time tracking of metabolic parameters. When paired with AI algorithms, these systems can generate personalized, adaptive intervention plans, marking a shift from traditional, experience-based lifestyle guidance to a more precise, data-centric management model, which is crucial for long-term patient engagement and adherence. In drug discovery, AI-assisted virtual screening technology has accelerated the discovery and clinical translation of various novel targeted drugs. A typical example is the THR- $\beta$  agonist Resmetirom, in whose development AI-assisted virtual screening played a pivotal role in candidate selection and optimization, thereby accelerating its path to clinical application and supporting the principles of precision medicine. Despite these impressive advances, translating AI innovations into routine MASLD care continues to face considerable technical and structural obstacles. The opacity of complex models undermines clinical trust, while privacy regulations restrict the multi-center data sharing needed for robust generalization. Overcoming these barriers requires a concerted effort that integrates technical innovation with rigorous ethical and regulatory frameworks.



Future priorities should include developing XAI and privacy-preserving computation, alongside establishing standardized validation and regulatory pathways to ensure model safety and equity. In the long run, successful clinical integration will depend on comprehensive multi-center validation across diverse populations and rigorous cost-effectiveness analyses.

With the continuous advancement of technologies such as deep learning and quantum computing, as well as improvements in the performance of mobile sensing devices, the full-cycle management of MASLD will become more intelligent, accurate, and personalized, which will help build a more efficient chronic disease management system.

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## Conflict of interest

The authors have no conflict of interests related to this publication.

## Author contributions

Conception and design of the study (WZ, GS, JS), drafting of the manuscript, figure preparation, data visualization (WZ), provision of study materials (WZ, QZ, XyX, XY, XbX, HT, YY, WY, JX, GS, JS), and critical revisions of the manuscript (GS, JS). All authors approved the final version and publication of the manuscript.

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