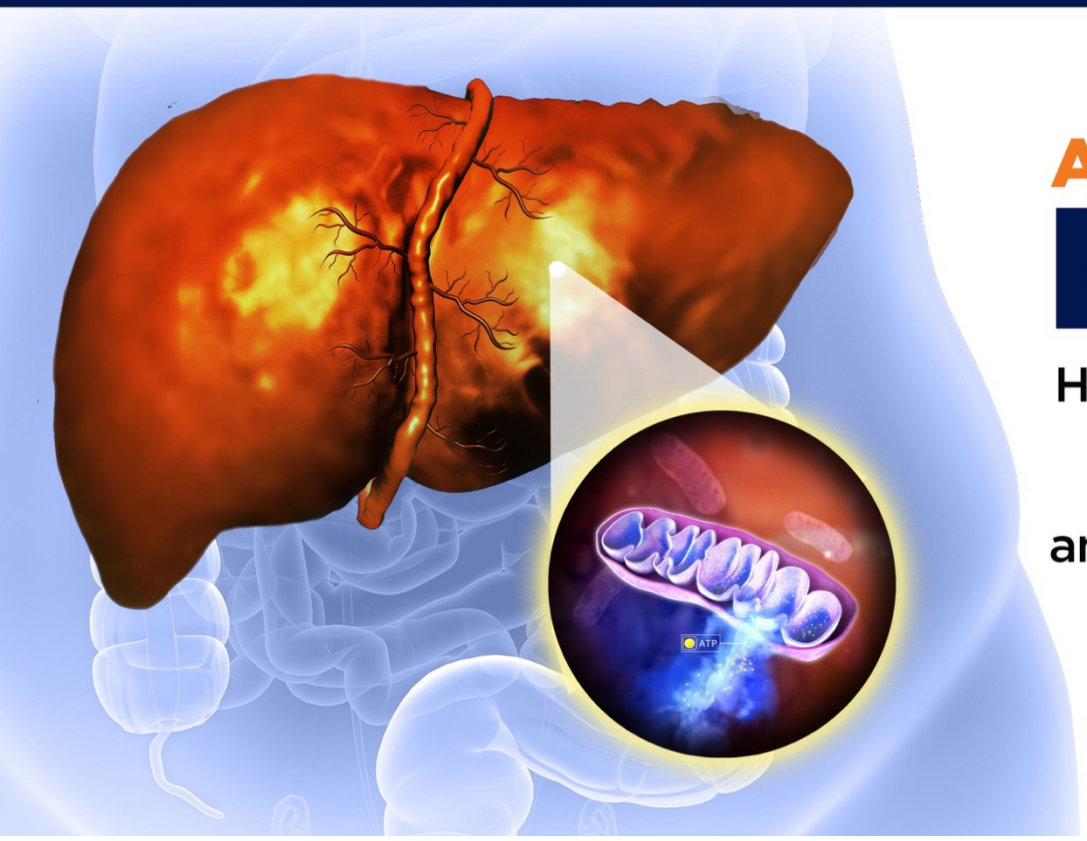

A NEW ERA IN MASH

How Disease-Specific Therapies Are Changing the Game and Best Practices for Clinical Integration

Suggested Readings

The Growing Burden of MASLD/MASH: A Call to Action

Angulo P, Kleiner DE, Dam-Larsen S, et al. Liver fibrosis, but no other histologic features, is associated with long-term outcomes of patients with nonalcoholic fatty liver disease. *Gastroenterology*. 2015;149:389-397.e10. doi:10.1053/j.gastro.2015.04.043

Banach M, Lewek J, Surma S, et al. The association between daily step count and all-cause and cardiovascular mortality: a meta-analysis. *Eur J Prev Cardiol*. 2023;30:1975-1985. doi:10.1093/eurjpc/zwad229

Castera L, Laouenan C, Vallet-Pichard A, et al. High prevalence of NASH and advanced fibrosis in type 2 diabetes: a prospective study of 330 outpatients undergoing liver biopsies for elevated ALT, using a low threshold. *Diabetes Care*. 2023;46:1354-1362. doi:10.2337/dc22-2048

Cusi K, Isaacs S, Barb D, et al. American Association of Clinical Endocrinology clinical practice guideline for the diagnosis and management of nonalcoholic fatty liver disease in primary care and endocrinology clinical settings: co-sponsored by the American Association for the Study of Liver Diseases (AASLD). *Endocr Pract*. 2022;28:528-562. doi:10.1016/j.eprac.2022.03.010

Dulai PS, Singh S, Patel J, et al. Increased risk of mortality by fibrosis stage in nonalcoholic fatty liver disease: systematic review and meta-analysis. *Hepatology*. 2017;65:1557-1565. doi:10.1002/hep.29085

En Li Cho E, Ang CZ, Quek J, et al. Global prevalence of non-alcoholic fatty liver disease in type 2 diabetes mellitus: an updated systematic review and meta-analysis. *Gut*. 2023;72:2138-2148. doi:10.1136/gutjnl-2023-330110

Harrison SA, Gawrieh S, Roberts K, et al. Prospective evaluation of the prevalence of non-alcoholic fatty liver disease and steatohepatitis in a large middle-aged US cohort. *J Hepatol*. 2021;75:284-291. doi:10.1016/j.jhep.2021.02.034

Ogurtsova K, da Rocha Fernandes JD, Huang Y, et al. IDF Diabetes Atlas: global estimates for the prevalence of diabetes for 2015 and 2040. *Diabetes Res Clin Pract*. 2017;128:40-50. doi:10.1016/j.diabres.2017.03.024

Stierman B, Afful J, Carroll MD, et al. National Health and Nutrition Examination Survey 2017–March 2020 prepandemic data files—development of files and prevalence estimates for selected health outcomes. *National Health Statistics Reports*. No. 158. National Center for Health Statistics. 2021. Accessed January 27, 2025. https://www.cdc.gov/nchs/data/nhsr/nhsr158-508.pdf

Vilar-Gomez E, Martinez-Perez Y, Calzadilla-Bertot L, et al. Weight loss through lifestyle modification significantly reduces features of nonalcoholic steatohepatitis. *Gastroenterology*. 2015;149:367-378.e5. doi:10.1053/j.gastro.2015.04.005

Williams CD, Stengel J, Asike MI, et al. Prevalence of nonalcoholic fatty liver disease and nonalcoholic steatohepatitis among a largely middle-aged population utilizing ultrasound and liver biopsy: a prospective study. *Gastroenterology*. 2011;140:124-131. doi:10.1053/j.gastro.2010.09.038

Wong RJ, Singal AK. Trends in liver disease etiology among adults awaiting liver transplantation in the United States, 2014-2019. *JAMA Netw Open*. 2020;3:e1920294. doi:10.1001/jamanetworkopen.2019.20294

Younossi ZM, Stepanova M, Rafiq N, et al. Pathologic criteria for nonalcoholic steatohepatitis: interprotocol agreement and ability to predict liver-related mortality. *Hepatology*. 2011;53:1874-82. doi:10.1002/hep.24268

Younossi ZM, Golabi P, Paik JM, et al. The global epidemiology of nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH): a systematic review. *Hepatology*. 2023;77:1335-1347. doi:10.1097/HEP.0000000000000004

Younossi ZM, Golabi P, Price JK, et al. The global epidemiology of nonalcoholic fatty liver disease and nonalcoholic steatohepatitis among patients with type 2 diabetes. *Clin Gastroenterol Hepatol.* 2024;22:1999-2010.e8. doi:10.1016/j.cgh.2024.03.006

Changing the MASH Paradigm With THR-β Agonists and Other Disease-Specific Therapies

Bano A, Chaker L, Plompen EPC, et al. Thyroid function and the risk of nonalcoholic fatty liver disease: The Rotterdam Study. *J Clin Endocrinol Metab*. 2016;101:3204-3211. doi:10.1210/jc.2016-1300

Bohinc BN, Michelotti G, Xie G, et al. Repair-related activation of hedgehog signaling in stromal cells promotes intrahepatic hypothyroidism. *Endocrinology*. 2014;155:4591-4601. doi:10.1210/en.2014-1302

Brandt SJ, Kleinert M, Tschöp MH, et al. Are peptide conjugates the golden therapy against obesity? *J Endocrinol.* 2018;238:R109-R119. doi:10.1530/JOE-18-0264

Bruinstroop E, Dalan R, Cao Y, et al. Low-dose levothyroxine reduces intrahepatic lipid content in patients with type 2 diabetes mellitus and NAFLD. *J Clin Endocrinol Metab*. 2018;103:2698-2706. doi:10.1210/jc.2018-00475

Bruinstroop E, Zhou J, Tripathi M, et al. Early induction of hepatic deiodinase type 1 inhibits hepatosteatosis during NAFLD progression. *Mol Metab*. 2021;53:101266. doi:10.1016/j.molmet.2021.101266

Chaves C, Bruinstroop E, Refetoff S, et al. Increased hepatic fat content in patients with resistance to thyroid hormone beta. *Thyroid*. 2021;31:1127-1134. doi:10.1089/thy.2020.0651

Chen Z, Yang L, Liu Y, et al. The potential function and clinical application of FGF21 in metabolic diseases. *Front Pharmacol*. 2022;13:1089214. doi:10.3389/fphar.2022.1089214

European Association for the Study of the Liver; European Association for the Study of Diabetes; European Association for the Study of Obesity. EASL-EASD-EASO clinical practice guidelines on the management of metabolic dysfunction-associated steatotic liver disease (MASLD): executive summary. *Diabetologia*. 2024;67:2375-2392. doi:10.1007/s00125-024-06196-3

Francque SM, Bedossa P, Ratziu V, et al. A randomized, controlled trial of the pan-PPAR agonist lanifibranor in NASH. *N Engl J Med*. 2021;385:1547-1558. doi:10.1056/NEJMoa2036205

Frias JP, Nauck MA, Van J, et al. Efficacy and safety of LY3298176, a novel dual GIP and GLP-1 receptor agonist, in patients with type 2 diabetes: a randomised, placebo-controlled and active comparator-controlled phase 2 trial. *Lancet*. 2018;392:2180-2193. doi:10.1016/S0140-6736(18)32260-8

Frias JP, De Block C, Brown K, et al. Tirzepatide improved markers of islet cell function and insulin sensitivity in people with T2D (SURPASS-2). *J Clin Endocrinol Metab*. 2024;109:1745-1753. doi:10.1210/clinem/dgae038

Geng L, Lam KSL, Xu A. The therapeutic potential of FGF21 in metabolic diseases: from bench to clinic. *Nat Rev Endocrinol*. 2020;16:654-667. doi:10.1038/s41574-020-0386-0

Harrison SA, Bashir MR, Guy CD, et al. Resmetirom (MGL-3196) for the treatment of non-alcoholic steatohepatitis: a multicentre, randomised, double-blind, placebo-controlled, phase 2 trial. *Lancet*. 2019;394:2012-2024. doi:10.1016/S0140-6736(19)32517-6

Harrison SA, Thang C, Bolze S, et al. Evaluation of PXL065 - deuterium-stabilized (R)-pioglitazone in patients with NASH: a phase II randomized placebo-controlled trial (DESTINY-1). *J Hepatol*. 2023;78:914-925. doi:10.1016/j.jhep.2023.02.004

Harrison SA, Ratziu V, Anstee QM, et al. Design of the phase 3 MAESTRO clinical program to evaluate resmetirom for the treatment of nonalcoholic steatohepatitis. *Aliment Pharmacol Ther.* 2024;59:51-63. doi:10.1111/apt.17734

Harrison S, Bedossa P, Guy CD, et al. A phase 3, randomized, controlled trial of resmetirom in NASH with liver fibrosis. *N Engl J Med*. 2024;390:497-509. doi:10.1056/NEJMoa2309000

Harrison SA, Frias JP, Neff G, et al. Efruxifermin significantly reduced liver fibrosis in MASH patients with F2–F3 fibrosis, with sustained improvement in liver injury and resolution of steatohepatitis over 96 weeks (HARMONY phase 2b study). Presented at: European Association for the Study of the Liver Congress 2024. Milan, Italy; June 5-8, 2024. Abstract LB-002.

Karim G, Bansal MB. Resmetirom: an orally administered, smallmolecule, liver-directed, β-selective THR agonist for the treatment of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis. *touchREV Endocrinol*. 2023;19:60-70. doi:10.17925/EE.2023.19.1.60

Lee E, Korf H, Vidal-Puig A. An adipocentric perspective on the development and progression of non-alcoholic fatty liver disease. *J Hepatol*. 2023;78:1048-1062. doi:10.1016/j.jhep.2023.01.024

Lefere S, Puengel T, Hundertmark J, et al. Differential effects of selective- and pan-PPAR agonists on experimental steatohepatitis and hepatic macrophages☆. *J Hepatol*. 2020;73:757-770. doi:10.1016/j.jhep.2020.04.025

Legaki A-I, Moustakas II, Sikorska M, et al. Hepatocyte mitochondrial dynamics and bioenergetics in obesity-related non-alcoholic fatty liver disease. *Curr Obes Rep*. 2022;11:126-143. doi:10.1007/s13679-022-00473-1

le Roux CW, Steen O, Lucas KJ, et al. Glucagon and GLP-1 receptor dual agonist survodutide for obesity: a randomised, double-blind, placebo-controlled, dose-finding phase 2 trial. *Lancet Diabetes Endocrinol*. 2024;12:162-173. doi:10.1016/S2213-8587(23)00356-X

Loomba R, Sanyal AJ, Kowdley KV, et al. Randomized, controlled trial of the FGF21 analogue pegozafermin in NASH. *N Engl J Med*. 2023;389:998-1008. doi:10.1056/NEJMoa2304286

Loomba R, Bedossa P, Grimmer K, et al. Denifanstat for the treatment of metabolic dysfunction-associated steatohepatitis: a multicentre, double-blind, randomised, placebo-controlled, phase 2b trial. *Lancet Gastroenterol Hepatol*. 2024;9:1090-1100. doi:10.1016/S2468-1253(24)00246-2

Loomba R, Hartman ML, Lawitz EJ, et al. Tirzepatide for metabolic dysfunction-associated steatohepatitis with liver fibrosis. *N Engl J Med*. 2024;391:299-310. doi:10.1056/NEJMoa2401943

Newsome PN, Buchholtz K, Cusi K, et al. A placebo-controlled trial of subcutaneous semaglutide in nonalcoholic steatohepatitis. *N Engl J Med*. 2021;384:1113-1124. doi:10.1056/NEJMoa2028395

O'Neil PM, Birkenfeld AL, McGowan B, et al. Efficacy and safety of semaglutide compared with liraglutide and placebo for weight loss in patients with obesity: a randomised, double-blind, placebo and active controlled, dose-ranging, phase 2 trial. *Lancet*. 2018;392:637-649. doi:10.1016/S0140-6736(18)31773-2

Ritter MJ, Amano I, Hollenberg AN. Thyroid hormone signaling and the liver. *Hepatology*. 2020;72:742-752. doi:10.1002/hep.31296

Romero-Gómez M, Lawitz E, Shankar RR, et al. A phase IIa active-comparator-controlled study to evaluate the efficacy and safety of efinopegdutide in patients with non-alcoholic fatty liver disease. *J Hepatol*. 2023;79:888-897. doi:10.1016/j.jhep.2023.05.013

Sanyal AJ, Bedossa P, Fraessdorf M, et al. A phase 2 randomized trial of survodutide in MASH and fibrosis. *N Engl J Med*. 2024;391:311-319. doi:10.1056/NEJMoa2401755

Saponaro F, Sestito S, Runfola M, et al. Selective thyroid hormone receptor-beta (TRβ) agonists: new perspectives for the treatment of metabolic and neurodegenerative disorders. *Front Med (Lausanne)*. 2020;7:331. doi:10.3389/fmed.2020.00331

Singh BK, Yen PM. A clinician's guide to understanding resistance to thyroid hormone due to receptor mutations in the TRα and TRβ isoforms. *Clin Diabetes Endocrinol*. 2017;3:8. doi:10.1186/s40842-017-0046-z

Sinha RA, Singh BK, Yen PM. Thyroid hormone regulation of hepatic lipid and carbohydrate metabolism. *Trends Endocrinol Metab*. 2014;25:538-545. doi:10.1016/j.tem.2014.07.001

Sinha RA, Yen PM. Thyroid hormone-mediated autophagy and mitochondrial turnover in NAFLD. *Cell Biosci*. 2016;6:46. doi:10.1186/s13578-016-0113-7

Sinha RA, Singh BK, Yen PM. Direct effects of thyroid hormones on hepatic lipid metabolism. *Nat Rev Endocrinol*. 2018;14:259-269. doi:10.1038/nrendo.2018.10

Taub R, Chiang E, Chabot-Blanchet M, et al. Lipid lowering in healthy volunteers treated with multiple doses of MGL-3196, a liver-targeted thyroid hormone receptor-β agonist. *Atherosclerosis*. 2013;230:373-380. doi:10.1016/j.atherosclerosis.2013.07.056

Rising to the Need to Improve Diagnosis in the Era of Disease-Specific Therapy

Abeysekera KWM, Valenti L, Younossi Z, et al. Implementation of a liver health check in people with type 2 diabetes. *Lancet Gastroenterol Hepatol*. 2024;9:83-91. doi:10.1016/S2468-1253(23)00270-4

Angulo P, Hui JM, Marchesini G, et al. The NAFLD fibrosis score: a noninvasive system that identifies liver fibrosis in patients with NAFLD. *Hepatology*. 2007;45:846-854. doi:10.1002/hep.21496

Anstee QM, Hallsworth K, Lynch N, et al. Real-world management of non-alcoholic steatohepatitis differs from clinical practice guideline recommendations and across regions. *JHEP Rep*. 2021;4:100411. doi:10.1016/j.jhepr.2021.100411

Anstee QM, Castera L, Loomba R. Impact of non-invasive biomarkers on hepatology practice: Past, present and future. *J Hepatol*. 2022;76:1362-1378. doi:10.1016/j.jhep.2022.03.026

Anstee QM, Berentzen TL, Nitze LM, et al. Prognostic utility of Fibrosis-4 Index for risk of subsequent liver and cardiovascular events, and all-cause mortality in individuals with obesity and/or type 2 diabetes: a longitudinal cohort study. *Lancet Reg Health Eur*. 2023;36:100780. doi:10.1016/j.lanepe.2023.100780

Boursier J, Tsochatzis EA. Case-finding strategies in non-alcoholic fatty liver disease. *JHEP Rep*. 2020;3:100219. doi:10.1016/j.jhepr.2020.100219

Boyle M, Tiniakos D, Schattenberg JM, et al. Performance of the PRO-C3 collagen neo-epitope biomarker in non-alcoholic fatty liver disease. *JHEP Rep.* 2019;1:188-198. doi:10.1016/j.jhepr.2019.06.004

Castera L, Forns X, Alberti A. Non-invasive evaluation of liver fibrosis using transient elastography. *J Hepatol*. 2008;48:835-847. doi:10.1016/j.jhep.2008.02.008

Castera L, Garteiser P, Laouenan C, et al. Prospective head-to-head comparison of non-invasive scores for diagnosis of fibrotic MASH in patients with type 2 diabetes. *J Hepatol*. 2024;81:195-206. doi:10.1016/j.jhep.2024.03.023

Chalasani N, Younossi Z, Lavine JE. The diagnosis and management of nonalcoholic fatty liver disease: practice guidance from the American Association for the Study of Liver Diseases. *Hepatology*. 2018;67:328-357. doi:10.1002/hep.29367

Chen VL, Morgan TR, Rotman Y, et al. Resmetirom therapy for metabolic dysfunction-associated steatotic liver disease: October 2024 updates to AASLD Practice Guidance. *Hepatology*. 2025;81:312-320. doi:10.1097/HEP.0000000000001112

Cusi K, Isaacs S, Barb D, et al. American Association of Clinical Endocrinology clinical practice guideline for the diagnosis and management of nonalcoholic fatty liver disease in primary care and endocrinology clinical settings: co-sponsored by the American Association for the Study of Liver Diseases (AASLD). *Endocr Pract*. 2022;28:528-562. doi:10.1016/j.eprac.2022.03.010

Daniels SJ, Leeming DJ, Eslam M, et al. ADAPT: an algorithm incorporating PRO-C3 accurately identifies patients with NAFLD and advanced fibrosis. *Hepatology.* 2019;69:1075-1086. doi:10.1002/hep.30163

Day J, Patel P, Parkes J, et al. Derivation and performance of standardized enhanced liver fibrosis (ELF) test thresholds for the detection and prognosis of liver fibrosis. *J Appl Lab Med.* 2019;3:815-826. doi:10.1373/jalm.2018.027359

Eddowes PJ, Sasso M, Allison M, et al. Accuracy of FibroScan controlled attenuation parameter and liver stiffness measurement in assessing steatosis and fibrosis in patients with nonalcoholic fatty liver disease. *Gastroenterology*. 2019;156:1717-1730. doi:10.1053/j.gastro.2019.01.042

European Association for the Study of the Liver. EASL Clinical Practice Guidelines on non-invasive tests for evaluation of liver disease severity and prognosis - 2021 update. *J Hepatol*. 2021;75:659-689. doi:10.1016/j.jhep.2021.05.025

European Association for the Study of the Liver (EASL); European Association for the Study of Diabetes (EASD); European Association for the Study of Obesity (EASO). EASL-EASD-EASO clinical practice guidelines on the management of metabolic dysfunction-associated steatotic liver disease (MASLD). *J Hepatol*. 2024;81:492-542. doi:10.1016/j.jhep.2024.04.031

Hagström H, Adams LA, Allen AM, et al. The future of International Classification of Diseases coding in steatotic liver disease: an expert panel Delphi consensus statement. *Hepatol Commun*. 2024;8:e0386. doi:10.1097/HC9.0000000000000386

Han MAT, Vipani A, Noureddin N, et al. MR elastography-based liver fibrosis correlates with liver events in nonalcoholic fatty liver patients: a multicenter study. *Liver Int.* 2020;40:2242-2251. doi:10.1111/liv.14593

Harrison SA, Bashir MR, Guy CD, et al. Resmetirom (MGL-3196) for the treatment of non-alcoholic steatohepatitis: a multicentre, randomised, double-blind, placebo-controlled, phase 2 trial. *Lancet*. 2019;394:2012-2024. doi:10.1016/S0140-6736(19)32517-6

Harrison SA, Ratziu V, Magnanensi J, et al. NIS2+™, an optimisation of the blood-based biomarker NIS4® technology for the detection of at-risk NASH: a prospective derivation and validation study. *J Hepatol.* 2023;79:758-767. doi:10.1016/j.jhep.2023.04.031

Harrison S, Bedossa P, Guy CD, et al. A phase 3, randomized, controlled trial of resmetirom in NASH with liver fibrosis. *N Engl J Med*. 2024;390:497-509. doi:10.1056/NEJMoa2309000

Kanwal F, Shubrook JH, Adams LA, et al. Clinical care pathway for the risk stratification and management of patients with nonalcoholic fatty liver disease. *Gastroenterology*. 2021;161:1657-1669. doi:10.1053/j.gastro.2021.07.049

Lazarus JV, Mark HE, Villota-Rivas M, et al. The global NAFLD policy review and preparedness index: Are countries ready to address this silent public health challenge? *J Hepatol*. 2022;76:771-780. doi:10.1016/j.jhep.2021.10.025

Loomba R, Wolfson T, Ang B, et al. Magnetic resonance elastography predicts advanced fibrosis in patients with nonalcoholic fatty liver disease: a prospective study. *Hepatology*. 2014;60:1920-1928. doi:10.1002/hep.27362

Loomba R, Sirlin CB, Ang B, et al. Ezetimibe for the treatment of nonalcoholic steatohepatitis: assessment by novel magnetic resonance imaging and magnetic resonance elastography in a randomized trial (MOZART trial). *Hepatology.* 2015;61:1239-1250. doi:10.1002/hep.27647

Loomba R, Sanyal AJ, Kowdley KV, et al. Factors associated with histologic response in adult patients with nonalcoholic steatohepatitis. *Gastroenterology*. 2019;156:88-95.e5. doi:10.1053/j.gastro.2018.09.021

McPherson S, Stewart SF, Henderson E, et al. Simple non-invasive fibrosis scoring systems can reliably exclude advanced fibrosis in patients with non-alcoholic fatty liver disease. *Gut*. 2010;59:1265-1269. doi:10.1136/gut.2010.216077

McPherson S, Hardy T, Dufour J-F, et al. Age as a confounding factor for the accurate non-invasive diagnosis of advanced NAFLD fibrosis. *Am J Gastroenterol*. 2017;112:740-751. doi:10.1038/ajg.2016.453

Mózes FE, Lee JA, Vali Y, et al. Performance of non-invasive tests and histology for the prediction of clinical outcomes in patients with non-alcoholic fatty liver disease: an individual participant data meta-analysis. *Lancet Gastroenterol Hepatol*. 2023;8:704-713. doi:10.1016/S2468-1253(23)00141-3

Newsome PN, Sasso M, Deeks JJ, et al. FibroScan-AST (FAST) score for the non-invasive identification of patients with non-alcoholic steatohepatitis with significant activity and fibrosis: a prospective derivation and global validation study. *Lancet Gastroenterol Hepatol.* 2020;5:362-373. doi:10.1016/S2468-1253(19)30383-8

Noureddin M, Yates KP, Vaughn IA, et al. Clinical and histological determinants of nonalcoholic steatohepatitis and advanced fibrosis in elderly patients. *Hepatology.* 2013;58:1644-1654. doi:10.1002/hep.26465

Noureddin N, Alkhouri N, Brown KA, et al. Driving nonalcoholic steatohepatitis forward using the FibroScan aspartate aminotransferase score, but obey the traffic lights. *Hepatology*. 2020;72:2228-2230. doi:10.1002/hep.31498

Noureddin M, Truong E, Gornbein JA, et al. MRI-based (MAST) score accurately identifies patients with NASH and significant fibrosis. *J Hepatol*. 2022;76:781-787. doi:10.1016/j.jhep.2021.11.012

Noureddin M, Charlton MR, Harrison SA, et al. Expert panel recommendations: practical clinical applications for initiating and monitoring resmetirom in patients with MASH/NASH and moderate to noncirrhotic advanced fibrosis. *Clin Gastroenterol Hepatol*. 2024;22:2367-2377. doi:10.1016/j.cgh.2024.07.003

Noureddin M, Truong E, Mayo R, et al. Serum identification of at-risk MASH: the metabolomics-advanced steatohepatitis fibrosis score (MASEF). *Hepatology*. 2024;79:135-148. doi:10.1097/HEP.0000000000000542

Ofosu A, Ramai D, Reddy M. Non-alcoholic fatty liver disease: controlling an emerging epidemic, challenges, and future directions. *Ann Gastroenterol*. 2018;31:288-295. doi:10.20524/aog.2018.0240

Patel J, Bettencourt R, Cui J, et al. Association of noninvasive quantitative decline in liver fat content on MRI with histologic response in nonalcoholic steatohepatitis. *Therap Adv Gastroenterol*. 2016;9:692-701. doi:10.1177/1756283X16656735

Polanco-Briceno S, Glass D, Stuntz M, et al. Awareness of nonalcoholic steatohepatitis and associated practice patterns of primary care physicians and specialists. *BMC Res Notes*. 2016;9:157. doi:10.1186/s13104-016-1946-1

Qadri S, Yki-Järvinen H. Surveillance of the liver in type 2 diabetes: important but unfeasible? *Diabetologia*. 2024;67:961-973. doi:10.1007/s00125-024-06087-7

Ratziu V, Goodman Z, Sanyal A. Current efforts and trends in the treatment of NASH. *J Hepatol*. 2015;62(suppl 1):S65-S75. doi:10.1016/j.jhep.2015.02.041

Ratziu V, Anstee QM, Wong VW-S, et al. An international survey on patterns of practice in NAFLD and expectations for therapies–The POP–NEXT project. *Hepatology*. 2022;76:1766-1777. doi:10.1002/hep.32500

Rinella ME, Lominadze Z, Loomba R, et al. Practice patterns in NAFLD and NASH: real life differs from published guidelines. *Therap Adv Gastroenterol*. 2016;9:4-12. doi:10.1177/1756283X15611581

Rinella ME, Neuschwander-Tetri BA, Siddiqui MS, et al. AASLD Practice Guidance on the clinical assessment and management of nonalcoholic fatty liver disease. *Hepatology*. 2023;77:1797-1835. doi:10.1097/HEP.0000000000000323

Sanyal AJ, Van Natta ML, Clark J, et al. Prospective study of outcomes in adults with nonalcoholic fatty liver disease. *N Engl J Med*. 2021;385:1559-1569. doi:10.1056/NEJMoa2029349

Sanyal AJ, Castera L, Wong VW-S. Noninvasive assessment of liver fibrosis in NAFLD. *Clin Gastroenterol Hepatol*. 2023;21:2026-2039. doi:10.1016/j.cgh.2023.03.042

Selvaraj EA, Mózes FE, Jayaswal ANA, et al. Diagnostic accuracy of elastography and magnetic resonance imaging in patients with NAFLD: a systematic review and meta-analysis. *J Hepatol.* 2021;75:770-785. doi:10.1016/j.jhep.2021.04.044

Siddiqui MS, Vuppalanchi R, Van Natta ML, et al. Vibration-controlled transient elastography to assess fibrosis and steatosis in patients with nonalcoholic fatty liver disease. *Clin Gastroenterol Hepatol*. 2019;17:156-163.e2. doi:10.1016/j.cgh.2018.04.043

Stern C, Castera L. Identification of high-risk subjects in nonalcoholic fatty liver disease. *Clin Mol Hepatol*. 2023;29(suppl):S196-S206. doi:10.3350/cmh.2022.0431

Sterling RK, Lissen E, Clumeck N, et al. Development of a simple noninvasive index to predict significant fibrosis in patients with HIV/HCV coinfection. *Hepatology*. 2006;43:1317-1325. doi:10.1002/hep.21178

Tapper EB, Castera L, Afdhal NH. FibroScan (vibration-controlled transient elastography): where does it stand in the United States practice. *Clin Gastroenterol Hepatol*. 2015;13:27-36. doi:10.1016/j.cgh.2014.04.039

Tapper EB, Lok AS-F. Use of liver imaging and biopsy in clinical practice. *N Engl J Med*. 2017;377:756-768. doi:10.1056/NEJMra1610570

Taylor RS, Taylor RJ, Bayliss S, et al. Association between fibrosis stage and outcomes of patients with nonalcoholic fatty liver disease: a systematic review and meta-analysis. *Gastroenterology*. 2020;158:1611-1625.e12. doi:10.1053/j.gastro.2020.01.043

Vali Y, Lee J, Boursier J, et al. Enhanced liver fibrosis test for the non-invasive diagnosis of fibrosis in patients with NAFLD: a systematic review and meta-analysis. *J Hepatol*. 2020;73:252-262. doi:10.1016/j.jhep.2020.03.036

Vali Y, Lee J, Boursier J, et al. Biomarkers for staging fibrosis and non-alcoholic steatohepatitis in non-alcoholic fatty liver disease (the LITMUS project): a comparative diagnostic accuracy study. *Lancet Gastroenterol Hepatol*. 2023;8:714-725. doi:10.1016/S2468-1253(23)00017-1

Integrating MASLD-/MASH-Specific Therapy Into Practice

Agency for Healthcare Quality and Research. The SHARE approach. Accessed January 27, 2025. https://www.ahrq.gov/health-literacy/professional-training/shared-decision/index.html

Aggarwal P, Noureddin M, Harrison S, et al. Nonalcoholic steatohepatitis (NASH) cirrhosis: a snapshot of therapeutic agents in clinical development and the optimal design for clinical trials. *Expert Opin Investig Drugs*. 2022;31:163-172. doi:10.1080/13543784.2022.2032640

Alkhouri N, Tincopa M, Loomba R, et al. What does the future hold for patients with nonalcoholic steatohepatitis: diagnostic strategies and treatment options in 2021 and beyond? *Hepatol Commun*. 2021;5:1810-1823. doi:10.1002/hep4.1814

Alkhouri N, Herring R, Kabler H, et al. Safety and efficacy of combination therapy with semaglutide, cilofexor and firsocostat in patients with non-alcoholic steatohepatitis: a randomised, open-label phase II trial. *J Hepatol*. 2022;77:607-618. doi:10.1016/j.jhep.2022.04.003.

Angulo P, Hui JM, Marchesini G, et al. The NAFLD fibrosis score: a noninvasive system that identifies liver fibrosis in patients with NAFLD. *Hepatology*. 2007;45:846-854. doi:10.1002/hep.21496

Attia SL, Softic S, Mouzaki M. Evolving role for pharmacotherapy in NAFLD/NASH. *Clin Transl Sci*. 2021;14:11-19. doi:10.1111/cts.12839

Chen VL, Morgan TR, Rotman Y, et al. Resmetirom therapy for metabolic dysfunction-associated steatotic liver disease: October 2024 updates to AASLD Practice Guidance. *Hepatology*. 2025;81:312-320. doi:10.1097/HEP.0000000000001112

Day J, Patel P, Parkes J, et al. Derivation and performance of standardized enhanced liver fibrosis (ELF) test thresholds for the detection and prognosis of liver fibrosis. *J Appl Lab Med.* 2019;3:815-826. doi:10.1373/jalm.2018.027359

de Franchis R, Bosch J, Garcia-Tsao G, et al. Baveno VII - renewing consensus in portal hypertension. *J Hepatol*. 2022;76:959-974. doi:10.1016/j.jhep.2021.12.022

Dufour J-F, Anstee QM, Bugianesi E, et al. Current therapies and new developments in NASH. *Gut*. 2022;71:2123-2134. doi:10.1136/gutjnl-2021-326874

European Association for the Study of the Liver; European Association for the Study of Diabetes; European Association for the Study of Obesity. EASL-EASD-EASO clinical practice guidelines on the management of metabolic dysfunction-associated steatotic liver disease (MASLD): executive summary. *Diabetologia*. 2024;67:2375-2392. doi:10.1007/s00125-024-06196-3

European Association for the Study of the Liver (EASL); European Association for the Study of Diabetes (EASD); European Association for the Study of Obesity (EASO). EASL-EASD-EASO clinical practice guidelines on the management of metabolic dysfunction-associated steatotic liver disease (MASLD). *J Hepatol*. 2024;81:492-542. doi:10.1016/j.jhep.2024.04.031

Fromenty B, Roden M. Mitochondrial alterations in fatty liver diseases. *J Hepatol*. 2023;78:415-429. doi:10.1016/j.jhep.2022.09.020

Gancheva S, Kahl S, Pesta D, et al. Impaired hepatic mitochondrial capacity in nonalcoholic steatohepatitis associated with type 2 diabetes. *Diabetes Care*. 2022;45:928-937. doi:10.2337/dc21-1758

Harrison S, Bedossa P, Guy CD, et al. A phase 3, randomized, controlled trial of resmetirom in NASH with liver fibrosis. *N Engl J Med*. 2024;390:497-509. doi:10.1056/NEJMoa2309000

Huang DQ, Wilson LA, Behling C, et al. Fibrosis progression rate in biopsy-proven nonalcoholic fatty liver disease among people with diabetes versus people without diabetes: a multicenter study. *Gastroenterology*. 2023;165:463-472.e5. doi:10.1053/j.gastro.2023.04.025

Jang H, Kim Y, Lee DH, et al. Outcomes of various classes of oral antidiabetic drugs on nonalcoholic fatty liver disease. *JAMA Intern Med*. 2024;184:375-383. doi:10.1001/jamainternmed.2023.8029

Kahl S, Ofstad AP, Zinman B, et al. Effects of empagliflozin on markers of liver steatosis and fibrosis and their relationship to cardiorenal outcomes. *Diabetes Obes Metab*. 2022;24:1061-1071. doi:10.1111/dom.14670

Krishnan A, Schneider CV, Hadi Y, et al. Cardiovascular and mortality outcomes with GLP-1 receptor agonists vs other glucose-lowering drugs in individuals with NAFLD and type 2 diabetes: a large population-based matched cohort study. *Diabetologia*. 2024;67:483-493. doi:10.1007/s00125-023-06057-5

Loomba R, Sanyal AJ, Kowdley KV, et al. Factors associated with histologic response in adult patients with nonalcoholic steatohepatitis. *Gastroenterology*. 2019;156:88-95.e5. doi:10.1053/j.gastro.2018.09.021

Loomba R, Abdelmalek MF, Armstrong MJ, et al. Semaglutide 2.4 mg once weekly in patients with non-alcoholic steatohepatitis-related cirrhosis: a randomised, placebo-controlled phase 2 trial. *Lancet Gastroenterol Hepatol*. 2023;8:511-522. doi:10.1016/S2468-1253(23)00068-7

McPherson S, Stewart SF, Henderson E, et al. Simple non-invasive fibrosis scoring systems can reliably exclude advanced fibrosis in patients with non-alcoholic fatty liver disease. *Gut*. 2010;59:1265-1269. doi:10.1136/gut.2010.216077

Newsome PN, Buchholtz K, Cusi K, et al. A placebo-controlled trial of subcutaneous semaglutide in nonalcoholic steatohepatitis. *N Engl J Med*. 2021;384:1113-1124. doi:10.1056/NEJMoa2028395

Noureddin M, Charlton MR, Harrison SA, et al. Expert panel recommendations: practical clinical applications for initiating and monitoring resmetirom in patients with MASH/NASH and moderate to noncirrhotic advanced fibrosis. *Clin Gastroenterol Hepatol*. 2024;22:2367-2377. doi:10.1016/j.cgh.2024.07.003

Patel J, Bettencourt R, Cui J, et al. Association of noninvasive quantitative decline in liver fat content on MRI with histologic response in nonalcoholic steatohepatitis. *Therap Adv Gastroenterol*. 2016;9:692-701. doi:10.1177/1756283X16656735

Polanco-Briceno S, Glass D, Stuntz M, et al. Awareness of nonalcoholic steatohepatitis and associated practice patterns of primary care physicians and specialists. *BMC Res Notes*. 2016;9:157. doi:10.1186/s13104-016-1946-1

Powell EE, Wong VW-S, Rinella M. Non-alcoholic fatty liver disease. *Lancet*. 2021;397:2212-2224. doi:10.1016/S0140-6736(20)32511-3

Ratziu V, Goodman Z, Sanyal A. Current efforts and trends in the treatment of NASH. *J Hepatol*. 2015;62(suppl 1):S65-S75. doi:10.1016/j.jhep.2015.02.041

Rinella ME, Lominadze Z, Loomba R, et al. Practice patterns in NAFLD and NASH: real life differs from published guidelines. *Therap Adv Gastroenterol*. 2016;9:4-12. doi:10.1177/1756283X15611581

Simon TG, Roelstraete B, Khalili H, et al. Mortality in biopsy-confirmed nonalcoholic fatty liver disease: results from a nationwide cohort. *Gut*. 2021;70:1375-1382. doi:10.1136/gutjnl-2020-322786

Sterling RK, Lissen E, Clumeck N, et al. Development of a simple noninvasive index to predict significant fibrosis in patients with HIV/HCV coinfection. *Hepatology*. 2006;43:1317-1325. doi:10.1002/hep.21178

Trauner M, Fuchs CD. Novel therapeutic targets for cholestatic and fatty liver disease. *Gut*. 2022;71:194-209. doi:10.1136/gutjnl-2021-324305

Wilding JPH, Batterham RL, Calanna S, et al. Once-weekly semaglutide in adults with overweight or obesity. *N Engl J Med*. 2021;384:989-1002. doi:10.1056/NEJMoa2032183

Vali Y, Lee J, Boursier J, et al. Enhanced liver fibrosis test for the non-invasive diagnosis of fibrosis in patients with NAFLD: a systematic review and meta-analysis. *J Hepatol*. 2020;73:252-262. doi:10.1016/j.jhep.2020.03.036

Vilar-Gomez E, Martinez-Perez Y, Calzadilla-Bertot L, et al. Weight loss through lifestyle modification significantly reduces features of nonalcoholic steatohepatitis. *Gastroenterology*. 2015;149:367-378.e5. doi:10.1053/j.gastro.2015.04.005