Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD)

Consultation on draft scope
Stakeholder comments table

30/04/25 – 01/06/25

Stakeholder	Page no.	Line no.	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
AstraZeneca UK Ltd	000	000	AstraZeneca UK Ltd. does not have any comments on the draft scope. The company looks forward to the consultation period for the guideline update.	Thank you for your comment.
Boehringer Ingelheim	000	000	Is the title of the Guideline, correct? This Guideline will not only cover MASLD but also MASH stages 1-3. Sections of the draft scope contain content relating to people with advanced liver fibrosis. By definition these people do not have MASLD but MASH. Neither will the late-stage pharmacological interventions be licensed for MASLD since the clinical trials have enrolled patients with MASH F2-3.	Thank you for your comment about terminology. The guideline and review questions will ensure appropriate use of MASLD and MASH terminology as defined in the literature.
Boehringer Ingelheim	000	000	As coding of MASH tends to be poor in Electronic Health records – which affects ability to identify patients and ensure they're being managed appropriately, would NICE consider including guidance about how to correctly code a MASLD or MASH patient once they've been identified	Thank you for your comment. This will be noted for consideration in the guideline development process.
Boehringer Ingelheim	000	000	Among the list of guidance that might be affected by this consultation, only those related to NITs imagining are included, but none on laboratory screening. We feel NICE should consider updating diagnostic algorithms to include, for example, pre-imaging NITs serum testing.	Thank you for your comment. The section of the scope referred to is for when there are other NICE guidance products that may be affected. The guideline committee will consider blood-based tests and composite scores alongside imaging technologies during development of the review protocols.
Boehringer Ingelheim	004	012	The question around relationship between alcohol consumption and MASLD outcomes" needs to specifically explore the thresholds and impact of different levels of alcohol consumption on MASLD progression and treatment response. It's impt for understanding patient subgroups and managing the disease	Thank you for your comment. This will be considered by the guideline committee during development of the review protocol.
British	000	000	First paragraph of the draft scope refers to making new	Thank you for your comment. The subgroup of people with

Association for Nutrition and Lifestyle Medicine			recommendation or updating existing recommendations on lifestyle modifications for MASLD. This is welcome as the aetiology and progression of MASLD is largely lifestyle driven. Reducing liver fat through dietary and lifestyle modification requires improvement in insulin sensitivity and glycaemic control. It is therefore both inconsistent and unsafe for the scope to exclude updating 1.2.12 to 1.2.14. NICE NG246 Obesity and Weight Management Guidance published in January 2025 is restrictive in scope: it does not include up to date reviews on evidence relating to non-nutritive sweeteners, high glycaemic diets and specific nutrients which contribute to insulin resistance and fatty liver deposits. Nor does it include markers for insulin sensitivity or inflammation. Therefore, the recommendations in NG246 are suitable only for those who are overweight or obese but metabolically healthy. It is unsafe to refer to NG246 for improvements in metabolic health. Lean MASLD makes up to 20% of MASLD cases overall which reinforces that body mass is unreliable as a predictor for metabolic health. References: 1. Kenneally, S., Sier, J. H., & Moore, J. B. (2017). Efficacy of dietary and physical activity intervention in non-alcoholic fatty liver disease: A systematic review. *BMJ Open Gastroenterology, 4*(1), e000139. 2. Romero-Gómez, M., Zelber-Sagi, S., Martín, F., Bugianesi, E., & Soria, B. (2023). Nutrition could prevent or promote non-alcoholic fatty liver disease: An	lean MASLD has been noted for consideration by the guideline committee during development. The dietary supplements review (RQ4) will examine specific dietary supplements for MASLD. Recommendations from 1.2.12 to 1.2.14 have not been prioritised for review in this update. NICE has a large portfolio of guidance on these topics (see diet, nutrition and obesity and physical activity).It was considered important to prioritise areas of diagnosis and monitoring within this guideline update, in order for guidance to be available to coincide with the approval of new treatments for MASH.

			opportunity for intervention. *The BMJ, 383*, e075179. 3. Xia, Y., Wu, Q., Dai, H., Lv, J., Liu, Y., Sun, H., Jiang, Y., Chang, Q., Niu, K., & Zhao, Y. (2021). Associations of nutritional, lifestyle, and metabolic factors with non-alcoholic fatty liver disease: An umbrella review with more than 380,000 participants. *Frontiers in Nutrition, 8*, 642509. Maier S, Wieland A, Cree-Green M, Nadeau K, Sullivan S, Lanaspa MA, Johnson RJ, Jensen T. Lean NAFLD: an underrecognized and challenging disorder in medicine. Rev Endocr Metab Disord. 2021 Jun;22(2):351-366. doi: 10.1007/s11154-020-09621-1. Epub 2021 Jan 3. PMID: 33389543; PMCID: PMC8893229.	
British Association for Nutrition and Lifestyle Medicine	000	000	Review of evidence for 1.2.15 and 1.2.16 should include a much wider field of lifestyle intervention than just exercise and alcohol.	Thank you for your comment. The scope includes review questions 4 and 5 which address dietary supplements and alcohol consumption respectively. Recommendations from 1.2.12 to 1.2.14 have not been prioritised for review in this update. NICE has a large portfolio of guidance on these topics (see diet, nutrition and obesity and physical activity).It was considered important to prioritise areas of diagnosis and monitoring within this guideline update, in order for guidance to be available to coincide with the approval of new treatments for MASH.
British Association for Nutrition and Lifestyle Medicine	005	1.1.1	Should stipulate that while MASLD is often associated with obesity and overweight, about 20% of cases are classified as Lean MASLD. Reference:	Thank you for your comment. This subgroup has been noted for consideration by the guideline committee during development.

			Maier S, Wieland A, Cree-Green M, Nadeau K, Sullivan S, Lanaspa MA, Johnson RJ, Jensen T. Lean NAFLD: an underrecognized and challenging disorder in medicine. Rev Endocr Metab Disord. 2021 Jun;22(2):351-366. doi: 10.1007/s11154-020-09621-1. Epub 2021 Jan 3. PMID: 33389543; PMCID: PMC8893229.	
British Association for Nutrition and Lifestyle Medicine	007	1.2.5	Propose expanding to: Refer adults and young people diagnosed with advanced liver fibrosis to a relevant specialist in hepatology and a dietitian or registered nutritionist for assessment of homocysteine status and nutritional interventions. Rationale: Homocysteine plays a significant role in hepatic fibrosis by promoting hepatic stellate cell (HSC) activation, increasing oxidative stress, and stimulating extracellular matrix deposition. Higher plasma homocysteine concentrations correlate with more severe liver fibrosis. References: 1. Zou, CG., Gao, SY., Zhao, YS. *et al.* Homocysteine enhances cell proliferation in hepatic myofibroblastic stellate cells. *J Mol Med* **87**, 75–84 (2009). https://doi.org/10.1007/s00109-008-0407-2 2. Suzuki A, Henao R, Reed MC, Nijhout HF, Tripathi M, Singh BK, Yen PM, Diehl AM, Abdelmalek MF. Lower hepatic *CBS* and *PEMT* expression in advanced NAFLD: inferencing strategies to lower homocysteine with a mathematical model. *Metab Target Organ*	Thank you for your comment. The evidence for recommendation 1.2.5 will be reviewed and recommendations updated, if appropriate.

			Damage. 2024;4:21. http://dx.doi.org/10.20517/mtod.2024.16	
British Association for Nutrition and Lifestyle Medicine	008		Fructose and digestible maltodextrins should be highlighted for particular review and advice: - Excessive fructose intake contributes to hepatic lipid accumulation and worsens insulin resistance, particularly in paediatric fatty liver disease. - Digestible maltodextrins, as high-GI carbohydrates, trigger blood glucose spikes, increase insulin secretion, and may lead to insulin resistance through lipogenesis, inflammation, and gut microbiota disruption. References: 1. Hrncir T, Trckova E, Hrncirova L. Synergistic Effects of Fructose and Food Preservatives on Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD): From Gut Microbiome Alterations to Hepatic Gene Expression. Nutrients. 2024 Oct 30;16(21):3722. doi: 10.3390/nu16213722. PMID: 39519554; PMCID: PMC11547954. 2. Jensen T, Abdelmalek MF, Sullivan S, Nadeau KJ, Green M, Roncal C, Nakagawa T, Kuwabara M, Sato Y, Kang DH, Tolan DR, Sanchez-Lozada LG, Rosen HR, Lanaspa MA, Diehl AM, Johnson RJ. Fructose and sugar: A major mediator of non-alcoholic fatty liver disease. J Hepatol. 2018 May;68(5):1063-1075. doi: 10.1016/j.jhep.2018.01.019. Epub 2018 Feb 2. PMID:	Thank you for your comment. The dietary supplements review (RQ4) will examine specific dietary supplements for MASLD where evidence meets inclusion criteria. Recommendations from 1.2.12 to 1.2.14 have not been prioritised for review in this update. NICE has a large portfolio of guidance on these topics (see diet, nutrition and obesity and physical activity). It was considered important to prioritise areas of diagnosis for identifying degree of fibrosis and monitoring within this guideline update, in order for guidance to be available to coincide with the approval of new treatments for MASH.

			29408694; PMCID: PMC5893377. 3. Page KA, Chan O, Arora J, Belfort-Deaguiar R, Dzuira J, Roehmholdt B, Cline GW, Naik S, Sinha R, Constable RT, Sherwin RS. Effects of fructose vs glucose on regional cerebral blood flow in brain regions involved with appetite and reward pathways. JAMA. 2013 Jan 2;309(1):63-70. doi: 10.1001/jama.2012.116975. Erratum in: JAMA. 2013 May 1;309(17):1773. PMID: 23280226; PMCID: PMC4076145. 4. Schwarz JM, Noworolski SM, Erkin-Cakmak A, Korn NJ, Wen MJ, Tai VW, Jones GM, Palii SP, Velasco-Alin M, Pan K, Patterson BW, Gugliucci A, Lustig RH, Mulligan K. Effects of Dietary Fructose Restriction on Liver Fat, De Novo Lipogenesis, and Insulin Kinetics in Children With Obesity. Gastroenterology. 2017 Sep;153(3):743-752. doi: 10.1053/j.gastro.2017.05.043. Epub 2017 Jun 1. PMID: 28579536; PMCID: PMC5813289.	
British Association for Nutrition and Lifestyle Medicine	008	1.2.12	Evidence for review on dietary advice to include low glycaemic and lower carbohydrate diets (than those recommended in the Eatwell Guide), which include mediterranean and ketogenic diets, to improve insulin sensitivity and reduce hepatic fat accumulation.	Thank you for your comment. Recommendations from 1.2.12 to 1.2.14 have not been prioritised for review in this update. NICE has a large portfolio of guidance on these topics (see diet, nutrition and obesity and physical activity). It was considered important to prioritise areas of diagnosis for identifying degree of fibrosis and monitoring within this

			The Eatwell Guide provides general dietary recommendations for a balanced diet, but there are several arguments against using it as a clinical model for individualised patient care for MASLD: 1. Lack of Personalisation – The Eatwell Guide is designed for population-wide health rather than individualised medical needs. MASLD patients often require tailored dietary interventions based on their metabolic profile, insulin resistance, and liver function. 2. Carbohydrate emphasis – The guide promotes starchy carbohydrates (e.g., bread, rice, pasta, potatoes), which may not be ideal for MASLD patients who benefit from lower carbohydrate intake to reduce liver fat accumulation. 3. Limited focus on specific nutrients – MASLD management often requires targeted nutrient modifications, such as higher omega-3 intake, lower fructose consumption, and specific micronutrient adjustments (e.g., vitamin D, choline). The Eatwell Guide does not emphasize these aspects. 4. Fats recommendations – The guide suggests reducing fat intake, but NMASLD patients may benefit from healthy fats (e.g., monounsaturated and polyunsaturated fats) to improve liver health. A Mediterranean-style diet is often recommended instead. 5. Insufficient guidance on highly processed foods – While the Eatwell Guide advises limiting high-fat, high-	guideline update, in order for guidance to be available to coincide with the approval of new treatments for MASH.

			sugar foods, it does not provide specific restrictions on ultra-processed foods, which are linked to worsening MASLD outcomes. It gives no advice on what constitutes minimally processed whole grains.	
British Association for Nutrition and Lifestyle Medicine	008	1.2.12	Intermittent Fasting and Time-Restricted Eating - Intermittent fasting can improve insulin sensitivity, reduce hepatic fat, and enhance metabolic function. - Long-term effects are still under investigation, but time-restricted eating may help optimize glucose regulation. References: 1. Marjot T, Tomlinson JW, Hodson L*, et al.* Timing of energy intake and the therapeutic potential of intermittent fasting and time-restricted eating in NAFLD. *Gut* 2023;**72:**1607-1619. 2. Yin C, Li Z, Xiang Y, Peng H, Yang P, Yuan S, Zhang X, Wu Y, Huang M, Li J. Effect of Intermittent Fasting on Non-Alcoholic Fatty Liver Disease: Systematic Review and Meta-Analysis. Front Nutr. 2021 Jul 12;8:709683. doi: 10.3389/fnut.2021.709683. PMID: 34322514; PMCID: PMC8310935.	Thank you for your comment. Recommendations from 1.2.12 to 1.2.14 have not been prioritised for review in this update. NICE has a large portfolio of guidance on these topics (see diet, nutrition and obesity and physical activity). It was considered important to prioritise areas of diagnosis for identifying degree of fibrosis and monitoring within this guideline update, in order for guidance to be available to coincide with the approval of new treatments for MASH. The NICE overweight and obesity management guideline NG246 (2025) considered the effectiveness of intermittent fasting in achieving and maintaining weight loss in adults living with overweight or obesity. The evidence review considered intermittent fasting, alternate day fasting and fasting for two days (e.g. 5:2 diet). Some evidence was identified on intermittent energy restriction. The evidence on this dietary approach was largely of low to very low quality and mainly came from only 1 or 2 trials per comparison. Due to these limitations, the committee did not draft specific recommendations on the use of these diets but noted that in practice intermittent energy restriction is now being used more commonly in practice, and

				therefore it would be useful to have further research on these diets. Based on this, the committee drafted a research recommendation to explore the effectiveness of these diets.
British Association for Nutrition and Lifestyle Medicine	008	1.2.12	Non-Nutritive Sweeteners. Some evidence suggests that artificial sweeteners may not be inert but have metabolic effects influencing liver fat accumulation and insulin sensitivity and markers of liver dysfunction. There is evidence that NNS can act via various routes, including: - Altering gut microbiota, which can influence liver fat accumulation. - Affect insulin sensitivity, potentially contributing to insulin resistance - Directly Modulating hepatic lipid metabolism and promoting fat deposition Some animal studies have shown that chronic consumption of NNS can lead to hepatic steatosis (fatty liver), even in the absence of excess caloric intake. Reference: Liauchonak I, Qorri B, Dawoud F, Riat Y, Szewczuk MR. Non-Nutritive Sweeteners and Their Implications on the Development of Metabolic Syndrome. Nutrients. 2019 Mar 16;11(3):644. doi: 10.3390/nu11030644. PMID: 30884834; PMCID: PMC6471792.	Thank you for your comment. Recommendations from 1.2.12 to 1.2.14 have not been prioritised for review in this update. NICE has a large portfolio of guidance on these topics (see diet, nutrition and obesity and physical activity). It was considered important to prioritise areas of diagnosis for identifying degree of fibrosis and monitoring within this guideline update, in order for guidance to be available to coincide with the approval of new treatments for MASH.
British Association for Nutrition and Lifestyle	008	1.2.12	Gut Microbiota and Inflammation. Dietary choices that support a healthy gut microbiome, including fibre-rich fruit and vegetables and low-GI foods, reduce inflammation associated with insulin resistance and fatty liver.	Thank you for your comment. Recommendations from 1.2.12 to 1.2.14 have not been prioritised for review in this update. NICE has a large portfolio of guidance on these topics (see diet, nutrition and obesity and physical activity). It was

Medicine			References: 1. Benedé-Ubieto R, Cubero FJ, Nevzorova YA. Breaking the barriers: the role of gut homeostasis in Metabolic-Associated Steatotic Liver Disease (MASLD). Gut Microbes. 2024 Jan-Dec;16(1):2331460. doi: 10.1080/19490976.2024.2331460. Epub 2024 Mar 21. PMID: 38512763; PMCID: PMC10962615. 2. Hamamah S, Iatcu OC, Covasa M. Dietary Influences on Gut Microbiota and Their Role in Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD). Nutrients. 2024 Dec 31;17(1):143. doi: 10.3390/nu17010143. PMID: 39796579; PMCID: PMC11722922.	considered important to prioritise areas of diagnosis for identifying degree of fibrosis and monitoring within this guideline update, in order for guidance to be available to coincide with the approval of new treatments for MASH.
British Association for Nutrition and Lifestyle Medicine	008	1.2.12	Counterweight diet model vs. Eatwell Guide. Structured weight management programmes (e.g., Counterweight) may offer superior benefits over general dietary recommendations like the Eatwell Guide, particularly for targeted weight loss and metabolic health. Counterweight diet was used by the DiRECT study, funded by the NHS, and recommends moderate starch as compared to the high starch Eatwell Guide. References: 1. The Counterweight Project Team. A new evidence-based model for weight management in primary care: the Counterweight Programme. J Hum Nutr Diet 2004; 17: 191-208.	Thank you for your comment. Recommendations from 1.2.12 to 1.2.14 have not been prioritised for review in this update. NICE has a large portfolio of guidance on these topics (see diet, nutrition and obesity and physical activity). It was considered important to prioritise areas of diagnosis for identifying degree of fibrosis and monitoring within this guideline update, in order for guidance to be available to coincide with the approval of new treatments for MASH. The NICE overweight and obesity management guideline NG246 (2025) considered the effectiveness and cost effectiveness of the Counterweight diet model in their evidence review for the effectiveness of different diets in

			2. Counterweight Project Team. Empowering Primary Care to tackle the obesity epidemic: The Counterweight Programme. European Journal of Clinical Nutrition 2005; 59: Supplement 1, S93-101. 3. Counterweight Project Team. Evaluation of the Counterweight Programme for obesity management in primary care: a starting point for continuous improvement. Br J Gen Pract 2008; 58: 548-54. 4. Counterweight Project Team. The implementation of the Counterweight Programme in Scotland, UK. Family Practice 2012; 29:i139- i144. 5. Lean et al. Feasibility and indicative results from a 12-month low-energy liquid diet treatment and maintenance programme for severe obesity. Br J Gen Pract 2013; e115-124.	achieving and maintaining weight loss. Please see recommendations 1.16.8 – 1.16.12 in this guideline.
British Association for Nutrition and Lifestyle Medicine	008	1.2.14	Sleep. Poor sleep quality and short sleep duration negatively affect glucose metabolism and may contribute to NAFLD progression. Optimizing sleep patterns supports overall metabolic function. References: 1. Mir HM, Stepanova M, Afendy H, Cable R, Younossi ZM. Association of Sleep Disorders with Nonalcoholic Fatty Liver Disease (NAFLD): A Population-based Study. J Clin Exp Hepatol. 2013 Sep;3(3):181-5. doi: 10.1016/j.jceh.2013.06.004. Epub 2013 Jul 2. PMID: 25755498; PMCID: PMC3940103.	Thank you for your comment. Recommendations from 1.2.12 to 1.2.14 on lifestyle modifications have not been prioritised for review in this update.

Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD)

Consultation on draft scope
Stakeholder comments table

30/04/25 – 01/06/25

			2. Okamura T, Hashimoto Y, Hamaguchi M, Obora A, Kojima T, Fukui M. Short sleep duration is a risk of incident nonalcoholic fatty liver disease: a population-based longitudinal study. J Gastrointestin Liver Dis. 2019 Mar;28(1):73-81. doi: 10.15403/jgld.2014.1121.281.alc. PMID: 30851175. Chung GE, Cho EJ, Yoo JJ, Chang Y, Cho Y, Park SH, Shin DW, Han K, Yu SJ. Nonalcoholic fatty liver disease is associated with the development of obstructive sleep apnea. Sci Rep. 2021 Jun 29;11(1):13473. doi: 10.1038/s41598-021-92703-0. PMID: 34188101; PMCID: PMC8241839.	
British Association for Nutrition and Lifestyle Medicine	008	1.2.15	Supplements for consideration include: - folate, vitamin B6, B12, and betaine lower homocysteine levels and reduce fibrosis risk - riboflavin (vitamin B2) is a fundamental cofactor for folate metabolism, including function of MTHFR (methylenetetrahydrofolate reductase) enzyme. Variants such as C677T reduce MTHFR efficiency and influence fibrosis progression. Optimising riboflavin status mitigates fibrosis risk, particularly in individuals with MTHFR polymorphisms - choline is necessary for lipid transport. Insufficient choline intake can lead to impaired very low-density lipoprotein (VLDL) secretion, contributing to liver dysfunction. In the United States choline is considered an essential nutrient and has a reference daily intake of between 425-550 gm daily	Thank you for your comment. The dietary supplements review (RQ4) will examine specific dietary supplements for MASLD where evidence meets inclusion criteria. These have been noted for consideration by the guideline committee during development of the review protocol.

			References: 1. Cai Liu, Hui Yao, Fang Wang, Effect of Nutritional Supplements for Reducing Homocysteine Levels in Healthy Adults: A Systematic Review and Network Meta-Analysis of Randomized Trials, *Nutrition Reviews*, 2025;, nuae191, https://doi.org/10.1093/nutrit/nuae191 2. Chen W, Xu M, Xu M, Wang Y, Zou Q, Xie S, Wang L. Effects of betaine on non-alcoholic liver disease. Nutr Res Rev. 2022 Jun;35(1):28-38. doi: 10.1017/S0954422421000056. Epub 2021 Apr 5. PMID: 33818349. 3. García-Minguillán, C.J., Fernandez-Ballart, J.D., Ceruelo, S. *et al.* Riboflavin status modifies the effects of methylenetetrahydrofolate reductase (MTHFR) and methionine synthase reductase (MTRR) polymorphisms on homocysteine. *Genes Nutr* **9**, 435 (2014). https://doi.org/10.1007/s12263-014-0435-1 4. Piras IS, Raju A, Don J, Schork NJ, Gerhard GS, DiStefano JK. Hepatic PEMT Expression Decreases with Increasing NAFLD Severity. Int J Mol Sci. 2022 Aug 18;23(16):9296. doi: 10.3390/ijms23169296. PMID: 36012560; PMCID: PMC9409182.	
British Society for Paediatric Endocrinolog	000	000	The question 2 for consultation is for adults. So we do not need to have any feedback.	Thank you for your comment. The consultation question on current pioglitazone and vitamin E use was indeed focused on adult practice.

y and Diabetes				
British Society of Gastrointestinal and Abdominal Radiology	004	002	What is the role of ultrasound based shear wave elastography as an alternative to Fibroscan and also US measurements of the fat attenuation coefficient of the liver?	Thank you for your comment. Non-invasive imaging tests will be considered by the guideline committee during drafting of the fibrosis assessment review protocols.
Cinnamon Days CIC	000	000	**Normal weight MASLD** The update to the MASLD Guideline should include specific reference to MASLD in lean individuals. It has been estimated that 25% of those with NAFLD are lean[1.] Leaner individuals may experience a faster rate of fibrosis progression than patients with a higher BMI [2.] The Guideline should include specific reference to MASLD in lean individuals in order to increase recognition and treatment of this condition in those who are lean. This is in line with recommendations made by the American Gastroenterology Association as described in 'AGA Clinical Practice Update: Diagnosis and Management of Non-Alcoholic Fatty Liver Disease (NAFLD) in Lean Individuals: Expert Review [3] 1. Long MT, Noureddin M, Lim JK. AGA Clinical Practice Update: Diagnosis and Management of Non-alcoholic Fatty Liver Disease in Lean Individuals: Expert Review.	Thank you for your comment. The subgroup of people with lean MASLD has been noted for consideration by the guideline committee during development.

			Gastroenterology. 2022 Sep;163(3):764-774.e1. doi: 10.1053/j.gastro.2022.06.023. Epub 2022 Jul 14. PMID: 35842345; PMCID: PMC9398982. 2. DiStefano JK, Gerhard GS. Metabolic dysfunction and non-alcoholic fatty liver disease risk in individuals with a normal body mass index. Curr Opin Gastroenterol. 2023 May 1;39(3):156-162. doi: 10.1097/MOG.0000000000000920. Epub 2023 Mar 1. PMID: 37144532; PMCID: PMC10201924. 3. Long MT, Noureddin M, Lim JK. AGA Clinical Practice Update: Diagnosis and Management of Non-alcoholic Fatty Liver Disease in Lean Individuals: Expert Review. Gastroenterology. 2022 Sep;163(3):764-774.e1. doi: 10.1053/j.gastro.2022.06.023. Epub 2022 Jul 14. PMID: 35842345; PMCID: PMC9398982.	
Cinnamon Days CIC	002	019	Table: What NICE plans to do for each area of the current guideline **Lifestyle Modification for MASLD** The draft scope specifies that it retain recommendations 1.2.12 to 1.2.14. 1.2.12 states that *Advice on physical activity and diet should be offered to people with NAFLD who are overweight or obese in line with NICE's guideline on overweight and obesity management.*	Thank you for your comment. The subgroup of people with lean MASLD has been noted for consideration by the guideline committee during development. Recommendations from 1.2.12 to 1.2.14 have not been prioritised for review in this update. NICE has a large portfolio of guidance on these topics (see diet, nutrition and obesity and physical activity).It was considered important to prioritise areas of diagnosis and monitoring within this guideline update, in order for guidance to be available to coincide with the approval of new treatments for MASH.

			1.2.14 specifies the following: *Consider the lifestyle interventions in NICE's guideline on overweight and obesity management for people with NAFLD regardless of their BMI* Diet plays a key role in the development of MASLD [2] and the dietary advice for those the MASLD, for both obese and lean individuals, should reflect the metabolic underpinnings of this condition[1]. More specific dietary advice aimed at improving metabolic health in this condition should be provided, rather than the more generic weight loss advice referenced in the NICE guideline on overweight and obesity as previously recommended. a) A review of dietary recommendations in MASLD should consider evidence on the specific impact of **fructose** on liver health, including the following: • Fructose has been recognised for several decades as being distinct from glucose in its unique ability to increase triglycerides and liver fat. A high fructose intake leads to the dysregulation of glucose, triglyceride, and cholesterol metabolism in the liver, increasing inflammation and driving the progression of non-alcoholic fatty liver disease [2]. • The single independent factor for the detection of	

			NAFLD in lean NAFLD was found in one study to be a higher juice and soft drink intake which contributed to a four-fold increase in the risk of NAFLD compared with individuals consuming less sugar-sweetened beverages.[3.] • Reducing fructose intake and metabolism can effectively treat obesity and NAFLD in men and women [4.] b) A review of dietary recommendations in MASLD should consider evidence on the impact of **ketogenic and lower carbohydrate diets** in this condition. There is evidence that in NAFLD patients with obesity, improvements in liver fat metabolism occur in response to ketogenic [5.] and low carbohydrate [6.] diets. , 1. Zarghamravanbakhsh P, Frenkel M, Poretsky L. Metabolic causes and consequences of non-alcoholic fatty liver disease (NAFLD). Metabol Open. 2021 Nov 16;12:100149. doi: 10.1016/j.metop.2021.100149. Erratum in: Metabol Open. 2023 Jan 21;17:100231. doi: 10.1016/j.metop.2023.100231. PMID: 34870138; PMCID: PMC8626571. 2. Lodge, M.; Dykes, R.; Kennedy, A. Regulation of Fructose Metabolism in Non-alcoholic Fatty Liver Disease. *Biomolecules* **2024**, *14*, 845.	

			https://doi.org/10.3390/biom14070845 3. Abid A, Taha O, Nseir W, et al. Soft drink consumption is associated with fatty liver disease independent of metabolic syndrome. J Hepatol 2009;51:918–24. 4. Simons, N.; Veeraiah, P.; Simons, P.; Schaper, N.C.; Kooi, M.E.; Schrauwen-Hinderling, V.B.; Feskens, E.J.M.; van der Ploeg, E.; Van den Eynde, M.D.G.; Schalkwijk, C.G.; et al. Effects of fructose restriction on liver steatosis (FRUITLESS); a double-blind randomized controlled trial. *Am. J. Clin. Nutr.* **2021**, *113*, 391–400 5. Luukkonen PK, Dufour S, Lyu K, et al. , Effect of a ketogenic diet on hepatic steatosis and hepatic mitochondrial metabolism in non-alcoholic fatty liver disease. Proc Natl Acad Sci U S A 2020; 117: 7347–7354. 6. Mardinoglu A, Wu H, Bjornson E, et al. , An integrated understanding of the rapid metabolic benefits of a carbohydrate-restricted diet on hepatic steatosis in humans. Cell Metab 2018; 27: 559–571	
Diabetes UK	000	000	Although the scope states that there are currently no plans to change the guidance on lifestyle modification for section 1.2.12 to 1.2.14 of the NAFLD guidance, we have a couple of comments that we would like to be taken into consideration: we feel that the wording of the guidance should be altered to reflect the appropriate language we would expect healthcare professionals to use with a patient in clinic - '1.2.12 Offer advice on physical activity and diet to people with NAFLD who are overweight or obese in line with NICE's guideline on	Thank you for your comment. NICE uses person-first language and this will be reflected consistently in the updated guideline.

			overweight and obesity management.' This should ideally say people 'living with overweight or obesity' instead. We would also recommend that there is more detail highlighting the importance of physical activity as a first line management for people living with MASLD, as per recent research: EASL-EASD-EASO Clinical Practice Guidelines on the management of metabolic dysfunction-associated steatotic liver disease (MASLD) - PubMed Hepatology The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases - PubMed	
Diabetes UK	003	011	We would like to raise a discussion regarding screening for MASLD/fibrosis in patients living with type 2 diabetes. We know that the risk factors for both conditions are very similar, and people living with diabetes receive annual health checks including blood tests for kidney function, but liver function/MASLD risk is not routinely checked as one of the annual care processes. The decision about whether this should occur will of course be a balance of the sensitivity and specificity of tests, potential for unnecessary further investigation if false positive, and cost effectiveness, and would of course also need to take into account the fact that LFTs can be normal in someone with liver	Thank you for your comment on screening for MASLD/fibrosis in people with type 2 diabetes. Following consultation feedback and the committee scoping discussion, systematic screening and case-finding approaches are outside the scope of this update, which focuses on assessment of people with confirmed MASLD. The guideline committee will consider high-risk subgroups (including people with diabetes) during development of the review protocols on identifying the degree of fibrosis and monitoring.

			disease, but given the high prevalence of MASLD in this population we believe it is worth discussion. Current NICE NAFLD guidance states that most cases of NAFLD are just diagnosed following incidental findings of abnormal LFT/abdominal ultrasound performed for other reasons. We wonder whether, given the potential benefit of early identification in terms of supporting someone with diet and exercise intervention, and the increased risk of advanced liver disease in someone living with type 2 diabetes vs the general population, routine screening of LFT as part of a MASLD risk assessment, such as the FIB-4, should occur. Some recent research suggests that this may be appropriate: A prospective study on the prevalence of MASLD in people with type-2 diabetes in the community. Cost effectiveness of screening strategies - PubMed Nonalcoholic Fatty Liver Disease Screening in Type 2 Diabetes Mellitus Patients in the Primary Care Setting - PMC Embedding assessment of liver fibrosis into routine diabetic review in primary care - PMC Implementation of a liver health check in people with type 2 diabetes - The Lancet Gastroenterology & Hepatology	

			Furthermore, the ADA standards of care in diabetes recommends screening for MASLD with a FIB-4 in initial and annual follow up: 4. Comprehensive Medical Evaluation and Assessment of Comorbidities: Standards of Care in Diabetes—2025 | Diabetes Care | American Diabetes Association And the EASD recommendations from Sep 2024 state that healthcare providers should look for MASLD with liver fibrosis in individuals with type 2 diabetes: EASL–EASD–EASO Clinical Practice Guidelines on the management of metabolic dysfunction-associated steatotic liver disease (MASLD) - Journal of Hepatology Changing the NICE guidance in this update would therefore be in line with the latest guidance in America and Europe.	
Hampshire Hospitals NHS Foundation Trust	000	000	The document uses the term Fibroscan repeatedly. Fibroscan is a commercial product and is one of many ways of diagnosisng fibrosis. Shearwave scanners are made by Ultrasound Manufacturers of which there are several. We use Shearwave in preference to Fibroscan for many reasons. Guidelines should encompass all means of testing for fibrosis and not refer to one commercial organisation.	Thank you for your comment. The scope only refers to this commercial product name in reference to the diagnostic guidance document. The guideline update will use generic terminology such as "transient elastography" and "shear wave elastography" to encompass all validated technologies from different manufacturers. Commercial product names may be used in protocols and searches to identify relevant literature.
Learning disabilities and autism programme	000	000	It is important to consider individuals who are known to have higher incidence of obesity such as those with a learning disability or are autistic. Identification of personalised needs should be considered as a core part of the pathway being	Thank you for your comment highlighting these equality considerations. These will be considered in guideline development alongside the completed equality and health inequalities assessment.

			offered as well as a proactive offer to vulnerable individuals in view of the diagnostic overshadowing which we know impacts and worsens life expectancy of these populations. Offering reasonable adjustments is a requirement of the Equality Act 2010.	
Learning disabilities and autism programme	000	000	It is going to be key to have guidance on whether semaglutide should/could be used – as even if not yet on NHS for this, there will be private / paid for use and primary/secondary care clinicians will need to be aware how to manage and support these patients.	Thank you for your comment. This guideline update will prioritise the areas of diagnosis for identifying the degree of fibrosis and monitoring. Specific treatment recommendations may be addressed through separate technology appraisals as these therapies become available. Technology appraisals will be incorporated into the guideline where possible.
NICE GP Reference Panel	000	000	We (the GP reference panel) received several comments on areas that the guideline does not currently intend to review as well as comments that can be addressed in the draft guideline questions. To provide continuity of subject matter I have listed the comments in the order of their position in the table P2 L19 but have identified the specific page/ line number (for the questions) when this is relevant. There is an additional comment on information, which does not appear in either the table or the questions.	Thank you for your comments.
NICE GP Reference Panel	000	000	We welcome the update of this key topic. It will be a very important, highly utilised guideline.	Thank you for your comment.
NICE GP Reference Panel	000	000	We like the brevity and clarity of the current guideline, but it does mean there are significant gaps that need to be addressed in this update.	Thank you for your comment.

Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD)

Consultation on draft scope
Stakeholder comments table

30/04/25 – 01/06/25

NICE GP Reference Panel	000	000	The current draft questions are relevant, but we feel that there are other significant questions and issues that the current guideline (and planned update) have not addressed.	Thank you for your comment.
NICE GP Reference Panel	000	000	Please keep the guidance (and CKS) as simple as possible as they will be translated into local pathways.	Thank you for your comment.
NICE GP Reference Panel	000	000	Workload: The workload for MASLD screening and investigating is already a significant burden. This includes phlebotomy, results analysis, processing, referral and sharing decisions and information. It has exponentially increased in the recent years probably due to increased awareness, more sophisticated pathways, and shift of work from secondary to primary care.	Thank you for your comment. The review questions on the diagnosis of MASLD are no longer in scope. Recommendations 1.1.4 to 1.1.7 will be stood down. Given the large number of people with MASLD, proactively identifying people with this condition would result in a significant increase in GP workload and demand for diagnostic services, with most patients not needing active treatment. Therefore, the scope has been narrowed to focus on people with confirmed MASLD who could benefit from new medicines to treat liver fibrosis.
NICE GP Reference Panel	000	000	Workload: Each new guidance comes with more unfunded work for primary care - how does NICE intend to address this?	Thank you for your comment. The review questions on the diagnosis of MASLD are no longer in scope. Recommendations 1.1.4 to 1.1.7 will be stood down. Given the large number of people with MASLD, proactively identifying people with this condition would result in a significant increase in GP workload and demand for diagnostic services, with most patients not needing active treatment. Therefore, the scope has been narrowed to focus on people with confirmed MASLD who could benefit from new medicines to treat liver fibrosis.
NICE GP Reference	000	000	Information: Individuals respond very differently to information about their health and guidelines need to take such variability	Thank you for your comment. This has been noted for discussion with the guideline committee during development.

Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD)

Consultation on draft scope
Stakeholder comments table

30/04/25 – 01/06/25

Panel			into account. Clinical trials, by their very nature, will recruit people who are likely to be more prepared to make changes and respond in a way medical research sees as rational. Barriers to behaviour changes can be complex and focusing on the consequences will detract from the time and resources we have available to help people manage their health holistically.	Limitations of the evidence (such as generalisability of clinical trial evidence to the population) will be considered by the committee during development of recommendations.
NICE GP Reference Panel	000	000	Information: In practice some people ignore their conditions and giving them an extra area to be worried about, their liver, may reinforce this tendency to denial.	Thank you for your comment.
NICE GP Reference Panel	000	000	Information: Please provide links to websites (for patients and doctors) that describes the disease and its (generally benign) prognosis.	Thank you for your comment. NICE provides additional links on the information for the public tab on the guideline website.
NICE GP Reference Panel	002	006	We ask that you look at MASLD in the context of all associated risks. A suggested review article: https://gut.bmj.com/content/73/4/691 If this is excluded from the update it is a missed opportunity to flag the associated risks and the importance of primary prevention.	Thank you for your comment. Recommendations on extra-hepatic conditions in section 1.2.10-1.2.11 will be retained and have not been prioritised for update. These recommendations address cardiovascular and other associated risks.
NICE GP Reference Panel	002	006	GPs are best positioned to coordinate the management of multimorbidity. One GP commented that in his patients (mostly S Asian) it is rare that liver disease will be the only health concern.	Thank you for your comment.
NICE GP Reference Panel	002	019	MASLD is a difficult condition for GPs to manage, usually we pick this up incidentally on a Liver ultrasound report. With increasing awareness of the condition and future treatments, however, this pathway may change substantially.	Thank you for your comment. These considerations have been noted for discussion by the guideline committee during development of the review protocols.

Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD)

Consultation on draft scope
Stakeholder comments table

30/04/25 – 01/06/25

NICE GP Reference Panel	002	019	Please clarify the risk factors for the development of MASLD	Thank you for your comment. The area of the current guideline on identifying groups at higher risk of MASLD has not been prioritised for review in this update and recommendations 1.1.1 and 1.1.2 will be stood down. NICE will continue to monitor this area for future updates.
NICE GP Reference Panel	002	019	Should we concentrate on high-risk patients rather than everybody with a small rise in ALT or other risk factors and normal tests? This is an important question in the light of the great burden on workload.	Thank you for your comment. The area of the current guideline on identifying groups at higher risk of MASLD has not been prioritised for review in this update and recommendations 1.1.1 and 1.1.2 will be stood down. NICE will continue to monitor this area for future updates.
NICE GP Reference Panel	002	019	There appears to be a fundamental gap in knowledge before you start answering the review questions on diagnostic accuracy and effectiveness. How do you make a diagnosis?	Thank you for your comment. The review questions on the diagnosis of MASLD are no longer in scope. Recommendations 1.1.4 to 1.1.7 will be stood down. Given the large number of people with MASLD, proactively identifying people with this condition would result in a significant increase in GP workload and demand for diagnostic services, with most patients not needing active treatment. Therefore, the scope has been narrowed to focus on people with confirmed MASLD who could benefit from new medicines to treat liver fibrosis.
NICE GP Reference Panel	002	019	We note this paper (Delphi consensus statement): https://journals.lww.com/hep/fulltext/2023/12000/a_multisociety_delphi_consensus_statement_on_new.28.aspx . Please incorporate this to provide clarity for GPs.	Thank you for your comment. This paper has been noted and the nomenclature changes will be addressed in the guideline.
NICE GP Reference Panel	002	019	If there is evidence that an ALT rise started after the commencements of can we assume that they don't need screening for MASLD?	Thank you for your comment. The review questions on the diagnosis of MASLD are no longer in the scope. The review questions on the diagnosis of MASLD are no longer in scope. Recommendations 1.1.4 to 1.1.7 will be stood down.

				Given the large number of people with MASLD, proactively identifying people with this condition would result in a significant increase in GP workload and demand for diagnostic services, with most patients not needing active treatment. Therefore, the scope has been narrowed to focus on people with confirmed MASLD who could benefit from new medicines to treat liver fibrosis.
NICE GP Reference Panel	002	019	Although you have advised us that specific guidance is not yet planned, we feel very strongly that general recommendations are needed. Several GPs commented that patients are already asking for treatments to address metabolic dysfunction/MASLD and we note that SGLT2 inhibitors and GLP1a +/-GIP drugs appear likely to show benefit.	Thank you for your comment. It was considered important to prioritise areas of diagnosis for identifying the degree of fibrosis and monitoring within this guideline update, in order for guidance to be available to coincide with the approval of new treatments. Specific treatment recommendations may be addressed through separate technology appraisals as these therapies become available. Technology appraisals will be incorporated into the guideline where possible.
NICE GP Reference Panel	003	009	There is currently no mention of liver ultrasound for adults, yet the international guidelines recommend steatosis needs to be confirmed on imaging (or biopsy). Should we be doing this in primary care?	Thank you for your comment. This guideline update will prioritise the area of diagnosis for identifying the degree of fibrosis. Given the large number of people with MASLD, proactively identifying people with this condition would result in a significant increase in GP workload and demand for diagnostic services, with most patients not needing active treatment. Therefore, the scope has been narrowed to focus on people with confirmed MASLD who could benefit from new medicines to treat liver fibrosis.
NICE GP Reference	003	009	Should obese people have their LFTs tested and how often?	Thank you for your comment. The area of the current guideline on identifying groups at higher risk of MASLD has

Panel				not been prioritised for review in this update and recommendations 1.1.1 and 1.1.2 will be stood down. NICE will continue to monitor this area for future updates. The review questions on the diagnosis of MASLD are no longer in the scope. The review questions on the diagnosis of MASLD are no longer in scope. Recommendations 1.1.4 to 1.1.7 will be stood down. Given the large number of people with MASLD, proactively identifying people with this condition would result in a significant increase in GP workload and demand for diagnostic services, with most patients not needing active treatment. Therefore, the scope has been narrowed to focus on people with confirmed MASLD who could benefit from new medicines to treat liver fibrosis.
NICE GP Reference Panel	003	009	We hope the guidance will specifically cover testing in the children. Will these be the same as adults? Blood tests are not done routinely in this population group.	Thank you for your comment. The guideline will cover children and young people. The guideline committee will discuss differences in testing for degree of fibrosis in children and young people with MASLD during development and make specific recommendations, if appropriate. The review questions on the diagnosis of MASLD are no longer in the scope. The review questions on the diagnosis of MASLD are no longer in scope. Recommendations 1.1.4 to 1.1.7 will be stood down. Given the large number of people with MASLD, proactively identifying people with this condition would result in a significant increase in GP workload and demand for diagnostic services, with most patients not needing active treatment. Therefore, the scope has been narrowed to focus on people with confirmed MASLD who could benefit from new medicines to treat liver fibrosis.

Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD)

Consultation on draft scope
Stakeholder comments table

30/04/25 – 01/06/25

NICE GP Reference Panel	003	011	Please identify which tests are helpful and which are not necessary. Some local pathways require large lists of tests to be performed.	Thank you for your comment. The diagnostic accuracy and effectiveness reviews examine multiple non-invasive tests for identifying degree of fibrosis.
NICE GP Reference Panel	003	011	Primary Care should be able to book all relevant tests to allow efficient referral. Even the simplest e.g. AST (for FIB4) aren't universally available without special request.	Thank you for your comment. These points about test accessibility have been noted for consideration during development. The diagnostic accuracy and effectiveness reviews examine multiple non-invasive tests for identifying degree of fibrosis.
NICE GP Reference Panel	003	011	Liver disease is important, but recommendations need to be rooted in the real world and acknowledge not just immediate cost benefit but also the opportunity costs in a creaking system without spare capacity.	Thank you for your comment. This has been noted for consideration by the guideline committee implementation team and resource impact team during development.
NICE GP Reference Panel	004	001	There were several requests for pragmatic guidance on this. The current guideline advises an ELF score yet, after nine years, many GPs still have no access to the required tests.	Thank you for your comment. These points about test accessibility have been noted for consideration during development. The guideline committee will consider non-invasive tests for fibrosis assessment during development of the review protocols.
NICE GP Reference Panel	004	001	ELF requires atypical tests not normally available or interpreted in general practice.	Thank you for your comment. These points about test accessibility have been noted for consideration during development. The guideline committee will consider non-invasive tests for fibrosis assessment during development of the review protocols.
NICE GP Reference Panel	004	002	Please include advice on FIB4 which is often used in local guidance.	Thank you for your comment. Multiple non-invasive scoring systems will be considered by the guideline committee during drafting of the fibrosis assessment review protocols.
NICE GP Reference Panel	004	002	Please include thresholds for referral after a FIB4	Thank you for your comment. Multiple non-invasive scoring systems, including relevant thresholds, will be considered by the guideline committee during drafting of the fibrosis

				assessment review protocols.
NICE GP Reference Panel	004	004	Please recommend that FIB4 (or other risk factor calculations) are incorporated into IT systems to save on the work of having to calculate these manually and transfer the results.	Thank you for your comment. This has been noted for consideration by the guideline committee and implementation team.
NICE GP Reference Panel	004	004	Please advise when/if Fibroscans should be used for risk assessment	Thank you for your comment. Non-invasive imaging tests will be considered by the guideline committee during drafting of the fibrosis assessment and monitoring review protocols.
NICE GP Reference Panel	004	006	Currently patients may not be on a formal disease register and may be lost to long term follow-up.	Thank you for your comment.
NICE GP Reference Panel	004	006	Please clarify the frequency of monitoring	Thank you for your comment. The monitoring review (RQ3) will examine evidence on different strategies where available, including frequency of monitoring.
NICE GP Reference Panel	004	006	Please clarify what procedures should be repeated including laboratory tests/ risk calculations and imaging (including fibroscans).	Thank you for your comment. Non-invasive tests and frequency of testing will be considered by the guideline committee during drafting of the monitoring review protocol.
NICE GP Reference Panel	004	006	Clarity is very important as health anxiety may lead to requests for significant extra monitoring and treatment. For some monitoring can also be a substitute for action to improve health.	Thank you for your comment. The monitoring review (RQ3) will examine evidence on different strategies where available, including frequency of monitoring.
NICE GP Reference Panel	004	010	When advising on lifestyle, weight loss and exercise together with reduced intake of alcohol need to be advocated. There is evidence for improving liver fibrosis by a weight loss of >10%. Please emphasise this in the guidance.	Thank you for your comment. Recommendations from 1.2.12 to 1.2.14 have not been prioritised for review in this update. NICE has a large portfolio of guidance on these topics (see diet, nutrition and obesity and physical activity).It was considered important to prioritise areas of diagnosis for identifying degree of fibrosis and monitoring within this guideline update, in order for guidance to be available to coincide with the approval of new treatments for MASH.

NICE GP Reference Panel	004	010	Dietary supplementation: please clarify this. Who will prescribe this?	Thank you for your comment. Dietary supplements are defined by the UK Food Standards Agency as 'any food the purpose of which is to supplement the normal diet and which is a concentrated source of a vitamin or mineral or other substance with a nutritional or physiological effect, alone or in combination and is sold in dose form. Dietary supplements are intended to correct nutritional deficiencies, maintain an adequate intake of certain nutrients, or to support specific physiological functions. They are not medicinal products and as such cannot exert a pharmacological, immunological or metabolic action'. Regarding prescribing – this will be considered by the committee during guideline development.
NICE GP Reference Panel	004	010	Please consider an emphasis on plant-based diet as a means to improve both inflammatory response and weight management.	Thank you for your comment. Recommendations from 1.2.12 to 1.2.14 have not been prioritised for review in this update. NICE has a large portfolio of guidance on these topics (see diet, nutrition and obesity and physical activity).It was considered important to prioritise areas of diagnosis for identifying degree of fibrosis and monitoring within this guideline update, in order for guidance to be available to coincide with the approval of new treatments for MASH. The NICE overweight and obesity management guideline NG246 (2025) completed an evidence review looked at the effectiveness of plant based diets in achieving and maintaining weight loss in adults living with overweight or

				obesity. No evidence was identified on the effectiveness of plant-based diets and the committee did not draft any recommendations or research recommendations for plant-based diets. The committee noted that plant-based diets are typically used to improve general wellbeing or due to sustainability or ethical issues, rather than for weight loss.
NICE GP Reference Panel	004	012	Several GPs commented that alcohol is a significant extra factor in risk in people with MASLD and we ask that the updated guidance better covers management of those where this is an issue.	Thank you for your comment. Review question 5 will aim to address this issue.
NICE GP Reference Panel	004	012	In reference to comment 11 the statement identifies a sub-definition for people with mixed pathology where alcohol is a more significant factor. https://journals.lww.com/hep/fulltext/2023/12000/a_multisociety_delphi_consensus_statement_on_new.28.aspx .	Thank you for your comment.
NICE GP Reference Panel	004	014	MASLD affects 1in 4 adult patients in Primary Care, far greater than diabetes or cardiovascular disease. Monitoring adds very significantly to the burden of chronic disease monitoring. There is overlap with other chronic conditions. This is a significant addition to the annual work of primary care in terms of phlebotomy, results analysis and processing, and referral. Please ensure that these costs are fully incorporated into the cost-effectiveness analysis.	Thank you for your comment. The primary focus is on detection of the degree of fibrosis in children, young people and adults with MASLD, not on treatment interventions. Therefore, the goal is to design a diagnostic model to identify the presence, risk, or stage of fibrosis. Following consultation feedback and the committee scoping discussion, systematic screening and case-finding approaches are outside the scope of this update, which focuses on assessment of people with confirmed MASLD. The guideline committee will consider high-risk subgroups (including people with diabetes) during development of the review protocols on identifying the degree of fibrosis and

				monitoring. Follow-up testing may be conducted to confirm findings suggested by the initial screening. The scope explicitly excludes treatment planning or therapeutic interventions; its role ends once a diagnostic or stratification decision has been made. The guideline committee will consider all relevant costs as part of the cost-effectiveness analysis.
NICE GP Reference Panel	004	014	Liver disease is important but recommendations need to be rooted in the real world and acknowledge not just immediate cost benefit but also the opportunity costs in a creaking system without spare capacity.	Thank you for your comment. This has been noted for consideration by the guideline committee, implementation team and resource impact team during development.
Norgine	004	001	The current guideline recommends considering the ELF test for assessing advanced liver fibrosis (recommendation 1.2.2). However, this test is not consistently available in all secondary care centres, which may lead to confusion or inconsistent application among clinicians. We suggest revising the recommendation to state: “Use the ELF test where available,” to better reflect current service variability and support practical implementation.	Thank you for your comment. These points about test accessibility have been noted for consideration during development. The guideline committee will consider non-invasive tests for fibrosis assessment during development of the review protocols.
Norgine	004	001	We would also like to suggest that the guideline consider explicitly recommending the use of non-invasive scoring systems such as the NAFLD Fibrosis Score (NFS) and FIB-4 to assess the risk of advanced liver fibrosis. This approach is already supported in the NICE Clinical Knowledge Summary (CKS) for NAFLD, which advises: “Assess the risk of advanced liver fibrosis — do not use	Thank you for your comment. Multiple non-invasive scoring systems will be considered by the guideline committee during drafting of the fibrosis assessment review protocols.

			routine liver blood tests. Consider using a non-invasive scoring system, such as the: NAFLD Fibrosis Score (NFS) — an intermediate or high score (greater than –1.455) suggests advanced liver fibrosis. Fibrosis-4 Score (FIB-4) — a score greater than 2.67 suggests advanced liver fibrosis." Including these tools in the main guideline would support broader clinical applicability, especially in settings where ELF testing is unavailable, and promote earlier identification of patients at risk.	
Novo Nordisk	000	000	2. The current guideline (NG49) recommends that, in secondary and tertiary care settings, pharmacological treatment with pioglitazone or vitamin E may be considered for adults with NAFLD (MASLD) and advanced liver fibrosis. The use of pioglitazone and vitamin E in the current guideline recommendations is off label. To what extent are the pioglitazone and vitamin E currently used in clinical practice for adults with advanced liver fibrosis and why? Please share any information about local clinical pathways you are aware of. NN response: We expect vitamin E and pioglitazone use to remain in secondary care as they are off-licence treatment options, albeit to a lesser extent as they are not commonly used.	Thank you for your comment providing information about current prescribing patterns.
Novo Nordisk	002	019	Suggest elaborating on 1.1.3 in current NAFLD Scope which currently reads 'Do not use routine liver blood tests to rule out NAFLD.' to 'Unexplained persistently abnormal liver blood tests should always be investigated, however normal liver	Thank you for your comment. Recommendations 1.1.1, 1.1.2 and 1.1.3 have not been prioritised for review in this update and will be stood down. NICE will continue to monitor this area for future updates.

			blood tests do not exclude MASLD or significant fibrosis.' (McPherson et al, 2022)	
Novo Nordisk	002	019	Consider aligning section 'Identifying people with advanced liver fibrosis' to EASL-EASD-EASO consensus guidelines, which suggests screening those with risk factors in primary care (T2D, obesity + one cardiometabolic risk factor, or persistently elevated liver enzymes) with Fib-4 first. If Fib-4 <1.3, remain in primary care and reassess at 1-3 years. If Fib-4 >2.67, refer to hepatology as high-risk of advanced fibrosis. If Fib-4 1.3-2.67, perform secondary test of either transient elastography (VCTE) or ELF (depending on local resources). Suggest including adjusted cut-offs for >65yoa population (EASL–EASD–EASO Clinical Practice Guidelines on the management of MASLD, 2024)	Thank you for your comment. The area of the current guideline on identifying groups at higher risk of MASLD has not been prioritised for review in this update and recommendations 1.1.1 and 1.1.2 will be stood down. NICE will continue to monitor this area for future updates. The guideline committee will consider non-invasive fibrosis tests such as FIB-4, and sequential testing approaches, during development of the review protocols.
Novo Nordisk	003	011	In Gruneau et al, 2023, the study suggests that non-invasive tests (NITs) such as FIB-4 and ELF in primary care, VCTE in specialist care, and liver biopsy to patients with high or indeterminate value of VCTE is less cost effective versus no testing. However, this does not take into account that once a patient is diagnosed, newer treatment that are currently being investigated in phase III trials, such as semaglutide and resmetirom, can slow the progression of liver fibrosis and hence would favourably impact the cost effectiveness of diagnostic tests, including NITs. This is echoed in two previous studies found that screening high-risk patients for MASLD was cost-effective, which contradicts the results from Gruneau et al (Zhang et al, 2015 and Nourredin et al, 2020). These studies modelled pharmacological treatments or weight loss	Thank you for your comment. This guideline update will prioritise the areas of diagnosis for identifying the degree of fibrosis and monitoring, rather than treatment interventions, as specific treatment recommendations may be addressed through separate technology appraisals as therapies become available. NICE is aiming to enhance coordination between technology appraisal timelines and the development of clinical guidelines.

			interventions that, conditional on test findings, affected the fibrosis disease progression (Zhang et al, 2015, Nourredin et al, 2020 and Tapper et al, 2015 & 2016).	
Novo Nordisk	003	019	Suggest expanding on 1.2.10 of the current NAFLD scope to 'Be aware that the leading cause of death in people with MASLD is cardiovascular disease.' Suggest also adding 'Weight loss and cardiovascular risk reduction are important points of management in those with MASLD and Type 2 Diabetes).' (McPherson et al, 2022)	Thank you for your comment. The area of the current guideline on extra-hepatic conditions has not been prioritised for review in this update and recommendations 1.2.10 and 1.2.11 will be retained.
Novo Nordisk	004	005	Conversations with hepatologists suggest that there is no consensus on the best method of monitoring MASH progression. However, some suggestions include follow-up VCTE every 6-12 months, liver blood tests and/or ELF. More commonly, hepatologists suggested a combined approached of looking at VCTE, ELF, and change in cardiometabolic risk factors (i.e.. Weight reduction, HbA1c change, BP change etc).	Thank you for your comment on monitoring approaches. Non-invasive tests and combinations of tests will be considered by the guideline committee during drafting of the monitoring review protocol.
Novo Nordisk	004	012	Suggest including the concept of MetALD to address the concept of relationship between alcohol consumption and MASLD. (Rinella et al, 2023)	Thank you for your comment.
Novo Nordisk	004	019	Conversations with hepatologists suggest that vitamin E and pioglitazone are used sparingly in secondary care due to concerns regarding evidence and side effects of pioglitazone.	Thank you for your comment providing information about current prescribing patterns.
Perspectum	002	019	Perspectum does not agree with the scope in its current state and feel that it is unduly restricted. There are now large population-based studies, epidemiology studies and systematic literature reviews, which show that similar to type 2 diabetes and metabolic syndrome (noted in recommendation 1.1.1) MASLD and MASH (previously NAFLD and NASH) are	Thank you for your comment. The area of the current guideline on identifying groups at higher risk of MASLD has not been prioritised for review in this update and will be stood down. NICE will continue to monitor this area for future updates.

			common in people who have obesity. Additionally, the prevalence of MASH, and MASH are similar in the overweight and obese population when compared to those with type 2 diabetes (*Quek., et al., Lancet Gastroenterol Hepatol. 2023. doi: 10.1016/S2468-1253(22)00317-X*; *Francque., et al., Lancet Gastroenterol Hepatol. 2023. doi: 10.1016/S2468-1253(22)00375-2).* Additionally, as noted in recommendation 1.2.11 NAFLD (MASLD) is a risk factor for cardiovascular events. Thus, an evaluation of MASLD for secondary prevention in the population following an adverse cardiovascular event is necessary as this is a high-risk group. There is new literature which shows that due to the shared risk factors (including type 2 diabetes, obesity and metabolic syndrome) there is a need to screen patients for NAFLD (MASLD), especially following an adverse event and hospitalisation (*Stahl., et al., J Am Coll Cardiol. 2019. doi:10.1016/j.jacc.2018.11.050*; *Josloff., J Cardiovasc Dev Dis. 2022. doi: 10.3390/jcdd9120419; Jackson., Nat Medicine. 2025. doi: 10.1038/s41591-025-03654-2*) **Therefore, we propose expansion of the scope to include patients with obesity and cardiovascular disease following an event as part of the high-risk groups requiring assessment**	
Perspectum	003	009	Perspectum agrees with the scope in its current state and for	Thank you for your comment.

			the rationale to review evidence following draft review question 1.	
Perspectum	003	011	Perspectum agrees with the scope in its current state and for the rationale to review evidence following draft review question 2	Thank you for your comment.
Perspectum	003	019	Perspectum does not agree with the scope in its current state. The extra-hepatic conditions listed in the scope should be expanded to include Major Adverse Cardiac Events (MACE) *(Jackson., Nat Medicine. 2025. doi: 10.1038/s41591-025-03654-2*). **Therefore, we propose expansion of the scope to include MACE to recommendation 1.2.10 and MACE in those who do not have type 2 diabetes as per 1.2.11 (NG49).**	Thank you for your comment. The area of the current guideline on extra-hepatic conditions has not been prioritised for review in this update and recommendations 1.2.10 and 1.2.11 will be retained. NICE guidance on cardiovascular risk is addressed by NG238
Perspectum	003	019	In light of evidence showing the increased risk for patient with MetALD, Perspectum agrees with the scope here and for the rationale to review evidence	Thank you for your comment.
Perspectum	003	019	Perspectum agrees with the scope in its current state and to retain the recommendations 1.3.1 and 1.3.2	Thank you for your comment.
Perspectum	003	019	Perspectum does not agree with the scope in its current state For recommendations 1.4.7 to 1.4.9, in addition to ELF, there are now new noninvasive markers which have been validated for use in both adults and paediatric patients (children and young adults) to monitor response to treatment (*Mojtahed., et al., Abdom Radiol (NY). 2019 doi: 10.1007/s00261-018-1701-2*; *Shumbayawonda., et al., Children (Basel). 2024 doi:*	Thank you for your comment. The guideline update proposes to stand down recommendations 1.4.1 to 1.4.9 regarding treatment with vitamin E and pioglitazone, and related treatment response recommendations. The guideline committee will consider the non-invasive tests for inclusion during development of the review protocols. This will include non-invasive tests for the monitoring of people with MASLD.

			10.3390/children11101230). This has also been shown in real world evidence studies in the United States following the approval of Rezdiffra *(Ravela., et al., Hepatol. Commun 2025. doi: 10.1097/HC9.0000000000000670).* In particular, mpMRI has been used to prescribe Rezdiffra in a number of patients and decreases in cT1 and liver fat content reflect treatment-induced histological improvements in MASH *(Alkhouri., et al., J Hepatol. 2025. doi: 10.1016/j.jhep.2024.08.031; Andersson., et al., CGH. 2025. doi: 10.1016/j.cgh.2025.03.003).* Furthermore, according to published literature, ELF is only available in a minority of centres (~25% in UK) and thus alternative methods should be reported to allow for better management of patients where this text is not available (*Ratziu., et al., Hepatology. 2022. doi: 10.1002/hep.32500*). **Therefore, we propose expansion of the scope to include the assessment and inclusion of other noninvasive tests, as alternatives or in addition to ELF, for the monitoring of patients.**	
Perspectum	004	002	Perspectum agrees with the scope in its current state and for the rationale to review evidence following draft review question 3	Thank you for your comment.
Perspectum	004	004	Whilst Perspectum agrees with the rationale to review evidence, we do not agree with the scope in its current state Studies in literature have shown that, for example, the rate of cumulative events in those with NASH (MASH) without fibrosis	Thank you for your comment. This guideline update will prioritise the areas of diagnosis for identifying the degree of fibrosis and monitoring. The review questions on the diagnosis of MASLD are no longer in scope. Recommendations 1.1.4 to 1.1.7 will be stood down. Given

Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD)

Consultation on draft scope
Stakeholder comments table

30/04/25 – 01/06/25

			is significantly higher compared to the general population *(Simon., Gut. 2022. doi: 10.1136/gutjnl-2021-325724).* Moreover, the likelihood of cardiovascular events and liver related hospitalisation is significant in patients with MASLD, both with and without advanced fibrosis *(Jackson., Nat Medicine. 2025. doi: 10.1038/s41591-025-03654-2).* **Therefore, we propose expansion of the scope to include assessment of clinical and cost effectiveness of assessment tools in identifying people with MASLD in those without advanced liver fibrosis, but who exhibit the risk factors described in 1.1.1.**	the large number of people with MASLD, proactively identifying people with this condition would result in a significant increase in GP workload and demand for diagnostic services, with most patients not needing active treatment. Therefore, the scope has been narrowed to focus on people with confirmed MASLD who could benefit from new medicines to treat liver fibrosis.
Perspectum	004	007	Perspectum agrees with the scope in its current state and for the rationale to review evidence following draft review of question 5	Thank you for your comment.
Primary Care Cardiovascular Society	001	021	The current scope of inclusion should remain the same	Thank you for your comment supporting the current scope coverage. This guideline update will prioritise the area of diagnosis for identifying the degree of fibrosis. The review questions on the diagnosis of MASLD are no longer in scope. Recommendations 1.1.4 to 1.1.7 will be stood down. Given the large number of people with MASLD, proactively identifying people with this condition would result in a significant increase in GP workload and demand for diagnostic services, with most patients not needing active treatment. Therefore, the scope has been narrowed to focus on people with confirmed MASLD who could benefit from new medicines to treat liver fibrosis.
Primary Care	002	004	There needs to be clearer guidance on the provision of	Thank you for your comment. This will be considered in

Cardiovascular Society			diagnostic services and access to these to prevent inequalities	guideline development alongside the completed equality and health inequalities assessment.
Primary Care Cardiovascular Society	005	020	Vitamin E is prescribed by secondary care. Pioglitazone is not widely used	Thank you for your comment providing information about current prescribing patterns.
Stanningley Pharma Ltd	004	009	The inclusion of dietary supplements in the draft scope is most welcome. Could this be expanded to make mention of the potential benefits of the increased protein intake made possible by the use modular protein supplements. These enable greatly increased protein supplementation without the often unneeded extra calories associated with more commonly used nutritional supplements.	Thank you for your comment. The dietary supplements review (RQ4) will examine the evidence on dietary supplements. During development of the review protocol the guideline committee will discuss the definition of a dietary supplement and the supplements for inclusion within the review protocol. Recommendations from 1.2.12 to 1.2.14 on dietary modifications have not been prioritised for review in this update.
Tawazun Health	000	000	***Comment on–*** *Are there any cost saving interventions or examples of innovative approaches that should be considered for inclusion in this guideline?* I would propose the assessment of specialist nurse-led FibroScan® services in primary care as an evidence-based, cost-effective, and innovative approach to liver disease assessment and triage. Evidence from the recent **EASL - LiverScreen Consortium**, presented at the European Liver Meeting (May 2025), involving over 30,000 patients (including UK cohorts), using ≥8KPa as increased stiffness, demonstrated a **66% improvement between the first and second FibroScan®** when delivered by trained specialist nurses in the primary care setting. These findings align with similar outcomes we observed in NHS England primary care cancer screening	Thank you for your comment. It has been noted that DG48 (FibroScan for assessing liver fibrosis and cirrhosis outside secondary and specialist care) may be affected by this update. The guideline committee will consider non-invasive tests and imaging technologies during development of the review protocols on diagnosis for identifying the degree of fibrosis. However, brief interventions and lifestyle modifications have not been prioritised for review in this update.

			pilots, we participated in, where primary care and patient engagement was high. Specialist nurse-delivered FibroScan not only facilitates efficient assessment of liver stiffness but also provides an opportunity for **brief behavioural interventions**. These interactions at the point of care can support lifestyle modifications and may look to improve patient outcomes without the need for secondary care referral in many cases. Importantly, there is on this evidence potential if **follow-up scans are performed in primary care** it may help to reduce unnecessary hepatology referrals by identifying the false positives—patients whose initial elevated liver stiffness scores may normalise with lifestyle changes or improved clinical control. This stratified approach allows for more accurate triaging, ensuring only patients requiring specialist input are referred, while others continue to be managed locally within primary care. This model proposes a shift from the current **blanket referral threshold of ≥8kPa**, which emerging evidence suggests may overwhelm hepatology services if applied universally without consideration of context or repeat measurements. In addition, LSM devices with a continuous attenuation parameter component which qualifies steatosis levels and enables the management of increased liver steatosis with no raised stiffness – optimising opportunities for lifestyle interventions to support other cardio-metabolic related conditions including Type 2 diabetes, obesity and cardiac disease.	

			Integrating this approach within the guideline could **optimise resource use, reduce costs, and enhance patient-centred care**. It also supports earlier intervention at the community level and aligns with NHS priorities on prevention and workforce optimisation. I would recommend this further evidenced intervention be considered for cost analysis assessment.	
Tawazun Health	002	019	**Comment on Draft Scope – Consideration of Post-Menopausal Women in High-Risk Groups for MASLD** The current draft scope does not recommend any expansion of the identified high-risk groups for MASLD (Metabolic dysfunction-associated steatotic liver disease). However, this appears to be at odds with the Equalities and Health Inequalities Assessment, which clearly states: “Menopausal status is associated with approximately 2.4-fold higher odds of MASLD. Women aged >50 years have increased odds of advanced fibrosis due to MASLD even after adjustment for covariates. The risk of severe fibrosis is elevated even in normal-weight post-menopausal women with MASLD compared to normal-weight pre-menopausal women with MASLD.” Emerging clinical data, including NHS England liver transplant referral trends, indicate that post-menopausal women represent one of the fastest-growing cohorts being referred for liver transplantation due to MASLD-related advanced fibrosis and cirrhosis. Excluding this known risk group is a significant concern given the predicted rise of healthcare needs in this	Thank you for your comment. This will be considered in guideline development alongside the completed equality and health inequalities assessment. The area of the current guideline on identifying groups at higher risk of MASLD has not been prioritised for review in this update and recommendations 1.1.1 and 1.1.2 will be stood down. NICE will continue to monitor this area for future updates. During development of the review protocol on monitoring MALSD progression, the guideline committee will consider high risk subgroups that may need specific consideration, such as post-menopausal women.

			group in the future.	
Tawazun Health	002	019	**Comment on Draft Scope – Consideration of Post-Menopausal Women in High-Risk Groups for MASLD** Given that MASLD is a locatable, treatable, and reversible condition—particularly when detected early in primary care—excluding post-menopausal women from high-risk group definitions may inadvertently disadvantage this population. This could lead to delayed diagnosis and intervention, increasing the likelihood of progression to liver failure and the need for transplantation. Furthermore, existing disparities in organ allocation and outcomes between men and women compound this risk. Evidence from NHS Blood and Transplant has shown that women are less likely to receive liver transplants and tend to have poorer post-transplant outcomes compared to men (NHSBT Annual Report on Liver Transplantation, 2022). To align with principles of equity and preventative healthcare, I strongly recommend that the scope be revised to include post-menopausal women as a high-risk group. This would support earlier identification and management, reduce the burden of advanced liver disease, and address a growing inequality in liver health outcomes.	Thank you for your comment. This will be considered in guideline development alongside the completed equality and health inequalities assessment. The area of the current guideline on identifying groups at higher risk of MASLD has not been prioritised for review in this update and recommendations 1.1.1 and 1.1.2 will be stood down. NICE will continue to monitor this area for future updates. During development of the review protocol on monitoring MALSD progression, the guideline committee will consider high risk subgroups that may need specific consideration, such as post-menopausal women.
The British Association for the Study of the Liver	000	000	People with MASLD who are taking GLP-1 RAs: use of GLP-1 RAs and related drugs is now widespread with licensed indications for diabetes and obesity. Could this guideline consider 1) the impact on MASLD in the population if access	Thank you for your comment. This guideline update will prioritise the areas of diagnosis for identifying the degree of fibrosis and monitoring. Specific treatment recommendations may be addressed through separate technology appraisals

			to these these drugs was optimal according to a) licensed indication and b) NICE guidance for those conditions, 2) whether MASLD should be considered an obesity-related comorbidity when prescribing tirzepetide, 3) what the additional benefit of resmetirom would be if a patient is already taking a GLP-1 RA	as these therapies become available. Technology appraisals will be incorporated into the guideline where possible.
The British Association for the Study of the Liver	000	000	This guideline will be strongly affected by whether resmetirom and semaglutide obtain marketing authorisation in the UK. The licence(s) will probably determine the need for liver biopsy, and the use of liver biopsy should be covered in the NICE MASLD guideline.	Thank you for your comment. The diagnostic tests to be considered in the protocols and evidence, including liver biopsy, will be discussed by the guideline committee during guideline development.
The British Association for the Study of the Liver	004	007	The question can be considered in 2 parts 1) what is the most clinically and cost effective monitoring strategy to determine *rate* of MASLD progression.... 2) what is the most clinically and cost effective strategy to determine the risk of MASLD progression... The first is assessing disease severity longitudinally (which patients, in what setting, how, frequency), the second is trying to identify those patients at higher risk of disease progression at the outset – a more difficult but perhaps more important questions	Thank you for your comment. The draft review question wording has been edited. This point has been noted for consideration by the guideline committee. During protocol development, the guideline committee will discuss and specify the aims of monitoring they wish to consider (for example, monitoring to determine the *rate* of MASLD progression, or monitoring to determine the *risk* of MASLD progression).
The British Association for the Study of the Liver	004	009	Some guidance on the benefit of lifestyle interventions (nutritional advice, exercise/physical activity advice) would be helpful, including cost-effectiveness and how these interventions could be delivered	Thank you for your comment. Recommendations from 1.2.12 to 1.2.14 have not been prioritised for review in this update. NICE has a large portfolio of guidance on these topics (see diet, nutrition and obesity and physical activity).It was considered important to prioritise areas of diagnosis for identifying the degree of fibrosis and monitoring within this guideline update, in order for guidance to be available to

				coincide with the approval of new treatments for MASH.
The British Association for the Study of the Liver	004	010	Beyond dietary supplements, could NICE consider dietary therapy such as total dietary replacement (very low-calorie diet) in MASLD	Thank you for your comment. Recommendations from 1.2.12 to 1.2.14 have not been prioritised for review in this update. NICE has a large portfolio of guidance on these topics (see diet, nutrition and obesity and physical activity).It was considered important to prioritise areas of diagnosis for identifying degree of fibrosis and monitoring within this guideline update, in order for guidance to be available to coincide with the approval of new treatments for MASH. The NICE overweight and obesity management guideline NG246 (2025) considered the effectiveness of low-energy and very-low-energy diets in achieving and maintaining weight loss in adults living with overweight or obesity. Please see recommendations 1.16.8 – 1.16.12 in this guideline.
The British Association for the Study of the Liver	004	010	Could NICE consider whether lifestyle intervention is required *before* or *alongside* any pharmacotherapy for MASLD	Thank you for your comment. Recommendations from 1.2.12 to 1.2.14 have not been prioritised for review in this update. NICE has a large portfolio of guidance on these topics (see diet, nutrition and obesity and physical activity).It was considered important to prioritise areas of diagnosis for identifying degree of fibrosis and monitoring within this guideline update, in order for guidance to be available to coincide with the approval of new treatments for MASH.
The British Association for the Study of the Liver	004	019	Question for consultation re pioglitazone and vitamin E. The BASL MASLD SIG conducted a survey of members who agreed that, when considering liver-specific therapies in MASLD	Thank you for your comment providing information about current prescribing patterns.

			"There should not be a requirement for prior use of unlicensed drugs such as vitamin E, pioglitazone or others" [manuscript in preparation] This reflects that the evidence in favour of vitamin E is very limited and the formulations are not standardised. Pioglitazone as a treatment for diabetes is superseded by newer medications with better liver and cardiovascular profiles and more favourable side-effect profiles. If considering advice on off-label pharmacotherapy, the evidence to support use of GLP-1 RAs (semaglutide, tirzepetide) specifically for MASLD is stronger than for pioglitazone, even without a licence. No member surveyed used pioglitazone or vitamin E regularly in their clinical practice.	
The British Association for the Study of the Liver	005	001	NICE guidance on overweight and obesity, and diabetes, is likely to be affected by, and affect this guideline update	Thank you for your comment. All of these NICE guidelines are part of the cardiometabolic suite, and the guideline development teams work together to determine the impact on other NICE guidance.
UK Clinical Pharmacy Association	000	000	Is the Metabolic dysfunction-associated steatohepatitis (liver fibrosis) - resmetirom and semaglutide ID6458 review due before this, if so it would be useful to include this within the MASLD guideline review	Thank you for your comment. This guideline update will prioritise the areas of diagnosis for identifying the degree of fibrosis and monitoring, rather than treatment interventions, as specific treatment recommendations may be addressed through separate technology appraisals as therapies become available. NICE is working towards coordination between technology appraisal timelines and guideline development. Technology

				appraisals will be incorporated into the guideline where possible.
UK Clinical Pharmacy Association	000	000	Do we need to separate adult patients to those at increased risk such as diabetic or obese patients?	Thank you for your comment. The scope covers all adults with confirmed MASLD. The guideline committee will consider high risk subgroups during guideline development.
UK Clinical Pharmacy Association	000	000	1. Are there any cost saving interventions or examples of innovative approaches that should be considered for inclusion in this guideline? o Newer FibroScan machines (all of those currently listed on the EchoSens website https://www.echosens.com/fibroscan/) are now capable of giving a CAP score for liver steatosis assessment. This was not available on some older versions and is not mentioned in the existing NAFLG CG49 nor the FibroScan DG48. Review of the evidence validating this technology, and recommendations on the role in diagnostics/assessment, should be included in the updated guideline.	Thank you for your comment. This guideline update will prioritise the area of diagnosis for identifying the degree of fibrosis. The review questions on the diagnosis of MASLD are no longer in the scope.
UK Clinical Pharmacy Association	000	000	2. The current guideline (NG49) recommends that, in secondary and tertiary care settings, pharmacological treatment with pioglitazone or vitamin E may be considered for adults with NAFLD (MASLD) and advanced liver fibrosis. The use of pioglitazone and vitamin E in the current guideline recommendations is off label. To what extent are the pioglitazone and vitamin E currently used in clinical practice for adults with advanced liver fibrosis and why? Please share any information about local clinical pathways you are aware of. o Unlicensed use of pioglitazone and vitamin E is not uniformly adopted across the NHS due to unlicensed nature	Thank you for your comment providing information about current prescribing patterns.

			and uncertain clinical benefit/ADRs and predominant use in advanced liver fibrosis ≥F3. Those with pre-existing diabetes most likely to have had prior pioglitazone therapy. We are not aware of any supporting local NHS guidelines/pathways currently in place. o Seems to be a move away from vitamin E and pioglitazone especially with clinical trials on potential options that are more targeted and effective as well as licensed.	
UK Clinical Pharmacy Association	003	000	Do we need to consider other lipid lowering agents here such as ezetimibe or evolocumab for example	Thank you for your comment. Recommendations 1.3.1 and 1.3.2 will be retained and are not prioritised for review in this update.