Journal Pre-proof

A multi-society Delphi consensus statement on new fatty liver disease nomenclature

Mary E. Rinella, Jeffrey V. Lazarus, Vlad Ratziu, Sven M. Francque, Arun J. Sanyal, Fasiha Kanwal, Diana Romero, Manal F. Abdelmalek, Quentin M. Anstee, Juan Pablo Arab, Marco Arrese, Ramon Bataller, Ulrich Beuers, Jerome Boursier, Elisabetta Bugianesi, Christopher D. Byrne, Graciela E. Castro Narro, Abhijit Chowdhury, Helena Cortez-Pinto, Donna Cryer, Kenneth Cusi, Mohamed El-Kassas, Samuel Klein, Wayne Eskridge, Jiangao Fan, Samer Gawrieh, Cynthia D. Guy, Stephen A. Harrison, Seung Up Kim, Bart Koot, Marko Korenjak, Kris Kowdley, Florence Lacaille, Rohit Loomba, Robert Mitchell-Thain, Timothy R. Morgan, Elisabeth Powell, Michael Roden, Manuel Romero-Gómez, Marcelo Silva, Shivaram Prasad Singh, Silvia C. Sookoian, C. Wendy Spearman, Dina Tiniakos, Luca Valenti, Miriam B. Vos, Vincent Wai-Sun Wong, Stavra Xanthakos, Yusuf Yilmaz, Zobair Younossi, Ansley Hobbs, Marcela Villota-Rivas, Philip N. Newsome, senior, on behalf of the NAFLD Nomenclature consensus group

PII: S0168-8278(23)00418-X

DOI: https://doi.org/10.1016/j.jhep.2023.06.003

Reference: JHEPAT 9207

To appear in: *Journal of Hepatology*

Please cite this article as: Rinella ME, Lazarus JV, Ratziu V, Francque SM, Sanyal AJ, Kanwal F, Romero D, Abdelmalek MF, Anstee QM, Arab JP, Arrese M, Bataller R, Beuers U, Boursier J, Bugianesi E, Byrne CD, Castro Narro GE, Chowdhury A, Cortez-Pinto H, Cryer D, Cusi K, El-Kassas M, Klein S, Eskridge W, Fan J, Gawrieh S, Guy CD, Harrison SA, Kim SU, Koot B, Korenjak M, Kowdley K, Lacaille F, Loomba R, Mitchell-Thain R, Morgan TR, Powell E, Roden M, Romero-Gómez M, Silva M, Singh SP, Sookoian SC, Spearman CW, Tiniakos D, Valenti L, Vos MB, Wai-Sun Wong V, Xanthakos S, Yilmaz Y, Younossi Z, Hobbs A, Villota-Rivas M, Newsome PN, on behalf of the NAFLD Nomenclature consensus group, A multi-society Delphi consensus statement on new fatty liver disease nomenclature, *Journal of Hepatology* (2023), doi: https://doi.org/10.1016/j.jhep.2023.06.003.

A multi-society Delphi consensus statement on new fatty liver disease nomenclature

Authors:

Mary E. Rinella[1], Jeffrey V. Lazarus[2,3], Vlad Ratziu[4], Sven M. Francque[5,6], Arun J. Sanyal[7], Fasiha Kanwal[8,9], Diana Romero[2], Manal F. Abdelmalek[10], Quentin M. Anstee[11,12], Juan Pablo Arab[13,14,15], Marco Arrese[15,16], Ramon Bataller[17], Ulrich Beuers[18], Jerome Boursier[19], Elisabetta Bugianesi[20], Christopher D. Byrne[21,22], Graciela E. Castro Narro [16,23,24], Abhijit Chowdhury[25], Helena Cortez-Pinto[26], Donna Cryer[27], Kenneth Cusi[28], Mohamed El-Kassas[29], Samuel Klein[30], Wayne Eskridge[31], Jiangao Fan[32], Samer Gawrieh[33], Cynthia D. Guy[34], Stephen A. Harrison[35], Seung Up Kim[36], Bart Koot[37], Marko Korenjak[38], Kris Kowdley[39], Florence Lacaille[40], Rohit Loomba[41], Robert Mitchell-Thain[42], Timothy R. Morgan[43,44], Elisabeth Powell[45,46,47], Michael Roden[48,49,50], Manuel Romero-Gómez[51], Marcelo Silva[52], Shivaram Prasad Singh[53], Silvia C. Sookoian[15,54,55], C. Wendy Spearman[56], Dina Tiniakos[11,57] , Luca Valenti[58,59], Miriam B. Vos[60], Vincent Wai-Sun Wong[61], Stavra Xanthakos[62], Yusuf Yilmaz[63], Zobair Younossi[64], Ansley Hobbs[2], Marcela Villota-Rivas[65], Philip N Newsome[66,67] (senior)

on behalf of the NAFLD Nomenclature consensus group**.**

[1] University of Chicago, Pritzker School of Medicine, Chicago, Illinois, USA

[2] City University of New York Graduate School of Public Health and Health Policy (CUNY SPH), New York, New York, USA

[3] Barcelona Institute for Global Health (ISGlobal), Hospital Clinic, University of Barcelona, Barcelona, Spain

[4] Sorbonne Université, ICAN Institute for Metabolism and Nutrition, Hospital Pitié-Salpêtrière, Paris, France

[5] Department of Gastroenterology Hepatology, Antwerp University Hospital, Edegem, Belgium

[6] InflaMed Centre of Excellence, Laboratory for Experimental Medicine and Paediatrics, Translational Sciences in Inflammation and Immunology, Faculty of Medicine and Health Sciences, University of Antwerp, Wilrijk, Belgium

[7] Virginia Commonwealth University, Richmond, Virginia, USA

[8] Sections of Gastroenterology and Hepatology and Health Services Research, Department of Medicine, Baylor College of Medicine, Houston, Texas, USA

[9] VA HSR&D Center for Innovations in Quality, Effectiveness, and Safety (IQuESt), Michael E. DeBakey Veterans Affairs Medical Center, Houston, Texas, USA

[10] Mayo Clinic, Rochester, Minnesota, USA

[11] Translational & Clinical Research Institute, Newcastle University, Newcastle upon Tyne, UK

[12] Newcastle NIHR Biomedical Research Center, Newcastle upon Tyne Hospitals NHS Trust, Newcastle upon Tyne, UK

[13] Division of Gastroenterology, Department of Medicine, Schulich School of Medicine, Western University & London Health Sciences Centre, London, Ontario, Canada

[14] Department of Epidemiology and Biostatistics, Schulich School of Medicine, Western University, London, Ontario, Canada

[15] Department of Gastroenterology, School of Medicine, Pontificia Universidad Catolica de Chile, Santiago, Chile

[16] Latin American Association for the Study of the Liver (ALEH) Santiago, Chile

[17] Liver Unit, Hospital Clinic, Institut d'Investigacions Biomediques August Pi i Sunyer (IDIBAPS), Barcelona, Spain

[18] Department of Gastroenterology & Hepatology, Tytgat Institute for Liver and Intestinal Research, Amsterdam University Medical Centers, Location AMC, Amsterdam, The Netherlands

[19] Hepato-Gastroenterology and Digestive Oncology Department, Angers University Hospital, Angers, France & HIFIH Laboratory UPRES EA3859, SFR 4208, Angers University, Angers, France

[20] Department of Medical Sciences, University of Torino, Torino, Italy

[21] Nutrition and Metabolism, Faculty of Medicine, University of Southampton, Southampton, UK

[22] National Institute for Health and Care Research Southampton Biomedical Research Centre, University Hospital Southampton, Southampton, UK

[23] Hepatology and Transplant Unit, Hospital Médica Sur, Mexico City, Mexico

[24] Department of Gastroenterology, National Institute of Medical Sciences and Nutrition "Salvador Zubirán" Mexico City, Mexico

[25] Indian Institute of Liver and Digestive Sciences , Sonarpur, Kolkata, India

[26] Clínica Universitária de Gastrenterologia, Faculdade de Medicina, Universidade de Lisboa, Lisboa, Portugal

[27] Global Liver Institute, Washington, District of Columbia, USA

[28] Division of Endocrinology, Diabetes and Metabolism, The University of Florida, Gainesville, Florida, USA

[29] Endemic Medicine Department, Faculty of Medicine, Helwan University, Cairo, Egypt

[30] Washington University School of Medicine, St. Louis, Missouri, USA

[31] Fatty Liver Foundation, Boise, Idaho, USA

[32] Xinhua Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

[33] Division of Gastroenterology and Hepatology, Indiana University School of Medicine, Indianapolis, Indiana, USA

[34] Department of Pathology, Duke Health Systems, Durham, North Carolina, USA

[35] Radcliffe Department of Medicine University of Oxford, Oxford, UK

[36] Yonsei University College of Medicine, Seoul, Korea

[37] Department of Pediatric Gastroenterology, Emma Children's Hospital, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands

[38] European Liver Patients' Association, Brussels, Belgium

[39] Liver Institute Northwest Elson S. Floyd College of Medicine Washington State University Seattle, Washington, USA

[40] Hôpital Universitaire Necker-Enfants Maladies, Paris, France

[41] University of California, San Diego, San Diego, California, USA

[42] PBC Foundation, Liver Patients International, Edinburgh, Scotland

[43] Medical Service, VA Long Beach Healthcare System, Long Beach, California, USA

[44] Department of Medicine, University of California, Irvine, California, USA

[45] Centre for Liver Disease Research, Faculty of Medicine, The University of Queensland, Translational Research Institute, Brisbane QLD, Australia

[46] QIMR Berghofer Medical Research Institute, Herston QLD, Australia

[47] Department of Gastroenterology and Hepatology, Princess Alexandra Hospital, Brisbane QLD, Australia

[48] Department of Endocrinology and Diabetology, Medical Faculty and University Hospital Düsseldorf, Heinrich Heine University Düsseldorf, Düsseldorf, Germany

[49] Institute for Clinical Diabetology, German Diabetes Center, Leibniz Center for Diabetes Research at Heinrich Heine University Düsseldorf, Düsseldorf, Germany

[50] German Center for Diabetes Research, Partner Düsseldorf, München-Neuherberg, Germany

[51] Digestive Diseases and Ciberehd. Virgen del Rocio University Hospital, Institute of Biomedicine of Seville (CSIC/HUVR/US), University of Seville, Seville, Spain

[52] Austral University Hospital, Buenos Aires, Argentina

[53] Kalinga Gastroenterology Foundation, Cuttack, Odisha, India

[54] Clinical and Molecular Hepatology, Centro de Altos Estudios en Ciencias Humanas y de la Salud (CAECIHS), Universidad Abierta Interamericana, Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Buenos Aires, Argentina

[55] Universidad Maimónides, Ciudad Autónoma de Buenos Aires, Buenos Aires, Argentina

[56] Division of Hepatology, Department of Medicine, Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa

[57] Department of Pathology, Aretaieion Hospital, Medical School, National and Kapodistrian University of Athens, Athens, Greece

[58] Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Milan, Italy

[59] Biological Resource Center Unit, Precision Medicine lab, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico Milano, Milan, Italy

[60] Division of Gastroenterology, Hepatology and Nutrition, Department of Pediatrics, Emory University and Children's Healthcare of Atlanta, Atlanta, Georgia, USA

[61] Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong, China

[62] Division of Gastroenterology Hepatology and Nutrition, Cincinnati Children's, Department of Pediatrics, Director, Nonalcoholic Steatohepatitis Center, University of Cincinnati College of Medicine, Cincinnati, Ohio, USA

[63] Department of Gastroenterology, School of Medicine, Recep Tayyip Erdoğan University, Rize, Turkey

[64] Inova Medicine, Inova Health System, Falls Church, Virginia, USA

[65] Barcelona Institute for Global Health (ISGlobal), Hospital Clínic, University of Barcelona, Barcelona, Spain

[66] National Institute for Health Research, Biomedical Research Centre at University Hospitals Birmingham NHS Foundation Trust and the University of Birmingham, Birmingham, UK

[67] Centre for Liver & Gastrointestinal Research, Institute of Immunology and Immunotherapy, University of Birmingham, Birmingham, UK

Corresponding authors:

Professor Philip N Newsome

National Institute for Health Research Birmingham Biomedical Research Centre and Centre for Liver & Gastrointestinal Research

5th Floor Institute of Biomedical Research

University of Birmingham

Birmingham, B15 2TT

UK

p.n.newsome@bham.ac.uk

Professor Mary E. Rinella

University of Chicago, Pritzker School of Medicine

Chicago, Illinois 60637

USA

mrinella@bsd.uchicago.edu

Contributors:

Veeral Ajmeral; William Alazawi; Maryam Alkhatry; Naim Alkhouri; Alina Allen; Michael Allison; Khalid Alswat; Mario R. Alvares-da-Silva; Michele Alves-Bezerra; Matthew J. Armstrong; Diego Arufe; Pablo Aschner; Gyorgy Baffy; Meena Bansal; Pierre Bedossa; Renata Belfort; Thomas Berg; Annalisa Berzigotti; Michael Betel; Cristiana Bianco; Clifford Brass; Carol L. Brosgart; Elizabeth Matthews Brunt; Maria Buti; Steve Caldwell; Rotonya Carr; Teresa Casanovas; Laurent Castera; Cyrielle Caussy; Eira Cerda; Naga Chalasani; Wah Kheong Chan; Phunchai Charatcharoenwitthaya; Michael Charlton; Amanda Cheung; Daniela Chiodi; Ray Chung; David Cohen; Kathleen Corey; Helma P. Cotrim; Javier Crespo; Anuradha Dassanayake; Nicholas Davidson; Robert De Knegt; Victor De Ledinghen; Münevver Demir; Sebastian Diaz; Anna Mae Diehl; Bruce Dimmig; Melisa Dirchwolf; Ajay Duseja; Karel Dvorak; Mattias Ekstedt; Reda El Wakil; María Lucía Ferraz; Scott Friedman; Michael Fuchs; Amalia Gastaldelli; Anja Geerts; Andreas Geier; Marcos Girala; George Goh; Nicolas Goossens; Isabel Graupera; Hannes Hagström; Zachary Henry; Bela Hunyady; Alan Hutchison; Scott Isaacs; François Jornayvaz; Cynthia Kemp; Denise Kile; Won Kim; David Kleiner; Rohit Kohli; Marcelo Kugelmas; Joel Lavine; Mariana Lazo; Nathalie Leite; Adelina Lozano; Panu Luukkonen; Paula Macedo; Dina Mansour; Giulio Marchesini; Sebastián Marciano; Kim Martinez; Lyudmila Vladimirova Mateva; Jose M. Mato; Alexis McCary; Luca Miele; Ivana Mikolasevic; Veronica Miller; Rosalba Moreno; Cynthia Moylan; Atsushi Nakajima; Jean Charles Nault; Suzanne Norris; Mazen Noureddin; C.P. Oliveira; Arlin Ong; Martín Padilla; Raluca Pais; Arturo Panduro; Manas K. Panigrahi; George Papatheodoridis; Serena Pelusi; Marlene Pérez; Juanita Perez Escobar; Gianluca Perseghin; Mario Pessoa; Salvatore Petta; Massimo Pinzani; Monica Platon Lupsor; Atoosa Rabiee; Stefano Romeo; Yaron Rotman; Ian Rowe; Riina Salupere; Sanjaya Satapathy; Jörn M. Schattenberg; Wendy Schaufert; Bernd Schnabl; Lynn Seim; Lawrence Serfaty; David Shapiro; Ashwani K. Singal; Lubomir Skladany; Norbert Stefan; Jonathan Stine; Shikha Sundaram; Gianluca Svegliati-Baroni; Gyonzgi Szabo; Frank Tacke; Tawesak Tanwandee; Giovanni Targher; Norah Terrault;

Brent Tetri; Maja Thiele; Baron Tisthammer; Aldo Torre Delgadillo; Michael Trauner; Emmanuel Tsochatzis; Laurens Van Kleef; Saskia Van Mil; Lisa VanWagner; Jose Antonio Velarde Ruiz Velasco; Mette Vesterhus; Eduardo Vilar-Gomez; Kymberly Watt; Julia Wattacheril; Fonda Wilkins; José Willemse; Amany Zekry; Shira Zelber-Sagi

Conflicts of Interest:

Manal F. Abdelmalek consults, advises, and received grants from Bristol Myers Squibb, Hanmi, Intercept, Inventiva, and Madrigal. She consults and advises 89Bio, Merck, NGM Bio, Novo Nordisk, Sonic Incytes, and Theratechnologies. She is on the speakers' bureau for Chronic Liver Disease Foundation, Clinical Care Options, Fishawack, Medscape, and Terra Firma. She received grants from Allergan, Boehringer-Ingelheim, Celgene, Durect, Enanta, Enyo, Galmed, Genentech, Gilead, Novo Nordisk, Poxel, Target NASH, and Viking.

Quentin M. Anstee, on behalf of Newcastle University, consults for Alimentiv, Akero, AstraZeneca, Axcella, 89Bio, Boehringer Ingelheim, Bristol Myers Squibb, Galmed, GENFIT, Genentech, Gilead, GlaxoSmithKline, Hanmi, HistoIndex, Intercept, Inventiva, Ionis, IQVIA, Janssen, Madrigal, Medpace, Merck, NGM Bio, Novartis, Novo Nordisk, PathAI, Pfizer, Pharmanest, Prosciento, Poxel, RTI, Resolution Therapeutics, Ridgeline Therapeutics, Roche, Shionogi, and Terns. He is on the speakers' bureau for Fishawack, Integritas Communications, Kenes, Novo Nordisk, Madrigal, Medscape, and Springer Healthcare. He received grants from AstraZeneca, Boehringer Ingelheim, and Intercept. He holds intellectual property rights with Elsevier, Ltd.

Ramon Bataller is on the speakers' bureau for Abbvie and Gilead.

Ulrich Beuers consults for CSL Behring. He is on the speakers' bureau for Abacus and Zambon.

Elisabetta Bugianesi advises Boehringer Ingleheim, MSD, and Novo Nordisk.

Helena Cortez-Pinto consults and received grants from Novo Nordisk and Roche. She received grants from Eisai, Gilead, GMP-Orphan, and Intercept.

Kenneth Cusi Consults for Aligos, Arrowhead, AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, Covance, Lilly, Madrigal, Myovant, Novo Nordisk, Prosciento, Sagimet, and Siemens. He received grants from Echosens, Inventiva, LabCorp, Nordic Biosciences, and Target NASH.

Sven M. Francque consults and received grants from Astellas, Falk, GENFIT, Gilead, Glympse Bio, Janssen, Inventiva, Merck, Pfizer, and Roche. He consults for AbbVie, Actelion, Aelin Therapeutics, Allergan, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, Coherus, CSL Behring, Echosens, Eisai, ENYO, Galapagos, Galmed, Genetech, Intercept, Julius Clinical, Madrigal, Medimmune, NGM Bio, Novartis, Novo Nordisk, and Promethera.

Samer Gawrieh consults for Pfizer and TransMedics. He received grants from LiverIncytes, Viking, and Zydus.

Manuel Romero-Gómez advises and received grants from Novo-Nordisk and Siemens. He advises AbbVie, Alpha-sigma, Allergan, AstraZeneca, Axcella, Boehringer-Ingelheim, Bristol Myers Squibb, Gilead, Intercept, Inventia, Kaleido, MSD, Pfizer, Prosciento, Rubió, Shionogi, Sobi, and Zydus. He received grants from Echosens and Theratechnologies.

Cynthia D. Guy consults for 89Bio, CymaBay, HistoIndex, Madrigal, and NGM.

Stephen Harrison consults, advises, is involved with trials, received grants, and owns stock in Akero, Galectin, GENFIT, Hepion, and NGM Bio. He consults, advises, is involved with trials, and received grants from Axcella, Gilead, Intercept, Madrigal, and Poxel. He consults, advises, received grants, and owns stock in NorthSea Therapeutics. He consults, advises, and is involved with trials for Terns. He consults, advises, and received grants from HighTide, Novartis, Novo Nordisk, and Sagimet. He consults, advises, and owns stock in HistoIndex, Metacrine, and Sonic Incytes. He consults, received grants, and owns stock in Cirius. He consults, is involved with trials, and received grants from ENYO and Viking. He is involved with trials and received grants from Genentech. He consults and is involved with trials for Ionis. He consults and received grants from CiVi, CymaBay, Galmed, and Pfizer. He consults and owns stock in Hepta Bio. He consults and advises for Altimmune, Echosens North America, Foresite Labs, and Medpace. He advises and owns stock in ChronWell. He consults for AgomAb, Alentis, Aligos Therapeutics, Alimentiv, Blade, Bluejay, Boston Pharmaceuticals, Boxer Capital, Can-Fite BioPharma, the Chronic Liver Disease Foundation (CLDF), CohBar, Corcept, Fibronostics, Fortress Biotech, Galecto, Gelesis, GlaxoSmithKline, GNS Healthcare, GRI Bio, Hepagene, Indalo, Inipharm, Innovate Biopharmaceuticals, Kowa Research Institute, Merck, MGGM, NeuroBo, Nutrasource, Perspectum, Piper Sandler, Prometic (now Liminal BioSciences), Ridgeline Therapeutics, Silverback, and Zafgen (now Larimar). He advises for Arrowhead BVF Partners, Humana, and Pathai. He received grants from Bristol Myers Squibb, Conatus, Immuron, and Second Genome.

Samuel Klein advises Alnylam, Altimmune, and Merck.

Kris V. Kowdley advises, is on the speakers' bureau, and received grants from Gilead and Intercept. He advises, received grants, and owns stock in Inipharm. He advises and received grants from 89bio, CymaBay, GENFIT, Ipsen, Madrigal, Mirum, NGM Bio, Pfizer, Pliant, and Zeds. He advises Enact, HighTide, and Protagonist. He is on the speakers' bureau for AbbVie. He received grants from Boston Pharmaceuticals, Corcept, GlaxoSmithKline, Hanmi, Janssen, Novo Nordisk, Terns, and Viking.

Jefferey V. Lazarus consults for Novavax. He received grants from AbbVie, Gilead, MSD, and Roche Diagnostics.

Rohit Loomba consults and received grants from Arrowhead, AstraZeneca, Bristol Myers Squibb, Galmed, Gilead, Intercept, Inventiva, Ionis, Janssen, Lilly, Madrigal, Merck, NGM Bio, Novo

Nordisk, Pfizer, and Terns. He consults and owns stock in 89 Bio and Sagimet. Consults for Altimmune, Anylam, Amgen, CohBar, Glympse Bio, HighTide, Inipharm, Metacrine, Novartis, Regeneron, Theratechnologies, and Viking. He received grants from Boehringer-Ingelheim, Galectin Therapeutics, Hanmi, and Sonic Incytes. He co-founded and owns stock in LipoNexus.

Phillip Newsome consults, advises, is on the speakers' bureau, and received grants from Novo Nordisk. He consults and advises Boehringer Ingelheim, Bristol Myers Squibb, Gilead, GlaxoSmithKline, Intercept, Madrigal, Pfizer, Poxel, and Sun Pharma. He is on the speakers' bureau for AiCME.

Elizabeth Powell advises and received grants from Novo Nordisk

Vlad Ratziu consults and received grants from Intercept. He consults for Boehringer Ingelheim, Eny, Madrigal, NorthSea, Novo Nordisk, Poxel, and Sagimet. He received grants from Gilead.

Mary E. Rinella consults for Boehringer Ingelheim, CytoDyn, GlaxoSmithKline, Intercept, Madrigal, NGM Bio, and Sonic Incytes.

Michael Roden consults and received grants from Boehringer Ingelheim and Novo Nordisk. He consults for Lilly. He is on the speakers' bureau for AstraZeneca.

Arun J. Sanyal consults and advises Avant Santé and AstraZeneca. He consults and received grants from Akero, Bristol Myers Squibb, Intercept, Lilly, Madrigal, and Novo Nordisk. He consults and owns stock in Rivus. He consults for AGED Diagnostics, Albireo, Alnylam, Altimmune, Boehringer Ingelhiem, 89Bio, Echosense, Genentech, Gilead, GlaxoSmithKline, HistoIndex, Malinckrodt, Merck, NGM Bio, Novartis, PathAI, Pfizer, Poxel, Regeneron, Salix, Siemens, Surrozen, Takeda, Terns, and Zydus. He owns stock in Durect, Exhalenz, GENFIT, Indalo, Inversago, and Tiziana. He received royalties from Elsevier and Wolters Kluwer.

Marcelo Silva consults, advises, and received grants from Zydus. He received grants from Inventiva and MSD.

Dina Tiniakos consults for Clinnovate Health, ICON, Ionis, Inventiva, Merck, and Verily.

Luca Valenti consults and received grants from Gilead. He consults for AstraZeneca, Boehringer Ingelheim, MSD, Novo Nordisk, Pfizer, and Resalis Therapeutics.

Miriam Vos consults and advises Thiogenesis. She consults and received grants from Target Real World Evidence. She consults and owns stock in Intercept. She consults for Albireo, Boehringer Ingelheim, Lilly, Novo Nordisk, and Takeda. She received grants from Bristol Myers Squibb, Quest, and Sonic Incytes.

Vincent Wai-Sun Wong consults and received grants from Gilead. He consults for AbbVie, Boehringer Ingelheim, Echosens, Intercept, Inventiva, Novo Nordisk, Pfizer, Sagimet, and TARGET PharmaSolutions. He owns stock in Illuminatio Medical Technology.

Yusuf Yilmaz consults for Zydus. He advises Novo Nordisk. He is on the speakers' bureau for Echosens.

Zobair Younossi consults for Bristol Myers Squibb, Gilead, Intercept, Madrigal, Merck, Novartis, Novo Nordisk, Quest, Siemens, and Terns.

Keywords: Fatty liver disease, NAFLD, NASH, nomenclature, Delphi, MASLD, MetALD,

steatohepatitis, steatotic liver disease, alcohol, type 2 diabetes, cardiometabolic, nonalcoholic

Tables

Supplementary Tables

Figures:

Figure 5. Steatotic Liver Disease sub-classification

Figure 6. MASLD diagnostic criteria

Supplementary Figures

Supplementary Figure 1. NAFLD Nomenclature Result: Round 4 (Complete)

ABSTRACT (287/275 words)

The principal limitations of the terms nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH) are the reliance on exclusionary confounder terms and the use of potentially stigmatising language. This study set out to determine if content experts and patient advocates were in favour of a change in nomenclature and/or definition. **Methods:** A modified Delphi process was led by three large pan-national liver associations. Consensus was defined *a priori* as a supermajority (67%) vote. An independent committee of experts external to the nomenclature process made the final recommendation on the acronym and its diagnostic criteria. **Results:** A total of 236 panellists from 56 countries participated in four online surveys and two hybrid meetings. Response rates across the 4 survey rounds were 87%, 83%, 83% and 78%, respectively. 74% of respondents felt that the current nomenclature was sufficiently flawed to consider a name change. The terms 'non-alcoholic' and 'fatty' were felt to be stigmatising by 61% and 66% of respondents, respectively. Steatotic liver disease (SLD) was chosen as an overarching term to encompass the various aetiologies of steatosis. The term steatohepatitis was felt to be an important pathophysiological concept that should be retained. The name chosen to replace NAFLD was metabolic dysfunction-associated steatotic liver disease (MASLD). There was consensus to change the definition to include the presence of at least one of five cardiometabolic risk factors. Those with no metabolic parameters and no known cause were deemed to have cryptogenic SLD. A new category, outside pure MASLD, termed MetALD was selected to describe those with MASLD who consume greater amounts of alcohol per week (140 to 350 g/week and 210 to 420 g/week for females and males

respectively). **Conclusions:** The new nomenclature and diagnostic criteria are widely supported, non-stigmatising and can improve awareness and patient identification.

INTRODUCTION

Unified global approaches to nomenclature and disease definition are critical for increasing disease awareness, driving policy change, identifying those at risk, facilitating diagnosis and access to care. Language can create or exacerbate stigma, marginalise segments of the affected population and, ultimately, contribute to health inequalities. It has been known for many years that being overweight or obese is associated with hepatic steatosis, hepatocyte injury and liver inflammation and fibrosis. This was formally recognized by the term “nonalcoholic steatohepatitis” in 1980 by Jurgen Ludwig. [1] Subsequently, the term nonalcoholic fatty liver disease (NAFLD) was used to describe the histological spectrum of steatosis to steatohepatitis with its subtypes nonalcoholic fatty liver (NAFL) and nonalcoholic steatohepatitis (NASH). The histological classification was further expanded upon by various scoring systems categorising steatosis, disease activity and fibrosis.[2-4] This framework has served as the anchor for our current understanding of the disease, data on the burden of disease, and efforts to develop treatment for the condition.

While the nomenclature is widely used, it has always been appreciated that the term “nonalcoholic" did not accurately capture what the aetiology of the disease was, and notably, the term ‘fatty’ has been considered to be stigmatising by some. Furthermore, there are individuals with risk factors for NAFLD, such as type 2 diabetes, who consume more alcohol than the relatively strict thresholds used to define the nonalcoholic nature of the disease that are not adequately recognised by existing nomenclature, are excluded from trials and consideration for treatments.[5] Indeed, there is a recognition now that there are overlapping

biological processes which may contribute to both NAFLD and alcohol-related liver disease (ALD). All of these factors have led to growing dissatisfaction with the current nomenclature. This was summarised in a paper by Eslam *et al* in 2020 and led to the proposal to use the term metabolic dysfunction associated fatty liver disease (MAFLD), which includes patients with a fatty liver regardless of the amount and pattern of alcohol intake under this terminology.[6, 7] While MAFLD was accepted by some, concerns were raised about the mixing of aetiologies, continued use of the term 'fatty' considered stigmatising by many, restricting the population to those with 2 metabolic risk factors and allowance of more liberal alcohol use, thus impacting our understanding of natural history.[8-10] One area of particular concern was the potential negative impact of changes in diagnostic criteria for the disease in terms of biomarker and therapeutic development.[7, 9, 10]

These concerns led to a multi-stakeholder effort under the auspices of the American Association for Study of Liver Disease (AASLD) and the European Association for Study of the Liver (EASL) in collaboration with the Asociación Latinoamericana para el Estudio del Hígado (ALEH) with engagement of academic professionals from around the world including hepatologists, gastroenterologists, paediatricians, endocrinologists, hepatopathologists and public health and obesity experts along with colleagues from industry, regulatory agencies and patient advocacy organisations to resolve these concerns and develop a consensus on a change in nomenclature and the diagnostic criteria for the condition. This manuscript summarises the methodology, including a multi-step Delphi process, the results of the process and provides the consensus recommendations endorsed by societies, patient advocacy groups, journals and industry for adoption by all stakeholders.

METHODS

Panel Generation and Statement Development

The panel for this Delphi study was generated through an iterative, inclusive process involving diverse liver organisations around the world (Table 1). The Steering Committee (n=36) was composed of two co-chairs (MER, PNN), representing AASLD and EASL, respectively and 34 other members nominated by their respective associations with a view to ensuring broad geographic representation.

The consensus process used a modified Delphi method [11-13] to incorporate input from the literature and a diverse group of content experts, practitioners, and patient advocates. The steering committee identified 5 areas deemed fundamental to the consideration of a revised nomenclature, namely: 1. What are issues with current nomenclature, and can they be addressed? 2. What is the importance of steatohepatitis in disease definition and endpoints? 3. How should the role of alcohol be accounted for? 4. How might name change impact disease awareness, clinical trials and regulatory approval pathways? and 5. Can an alternative name reduce heterogeneity and allow for future advances? Between late 2021 and early 2022, the steering committee was divided into six working groups, each with a designated lead (SMF, MER, PNN, AJS, VR, FK), responsible for reviews of the literature to inform development of draft statements for their assigned topic area: patient-centred perspective (SMF); pros and cons of the current nomenclature (MER); defining fatty liver disease in the setting of metabolic dysfunction (PNN); disease heterogeneity (AJS); histopathology (VR); and how to manage the role of alcohol in dual aetiology (FK). The preliminary draft statements were compiled and

shared with the larger steering committee for review, and the feedback was incorporated into a revised set of draft consensus statements **(Supplementary Table 1).**

Pan-national societies were asked to nominate additional experts and other stakeholders including patient advocacy organisations to be invited (n=267) to participate in the Delphi panel **(Figure 1)**. Nominating societies were instructed to select individuals actively engaged in NAFLD research or clinical practice of patients with NAFLD. Consensus was defined *a priori* as a supermajority (67%) vote. To increase geographic diversity in the Delphi panel, an additional 30 experts were invited to participate in R2. The characteristics, including demographics, professional expertise, and geographic representation, of Delphi panel participants (n=224) are summarised in **Table 1** and **Supplementary Table 2**.

Data Collection

The Delphi process comprised six components of online data collection (via the Qualtrics platform) and in-person discussions, including a first round (R1) survey (7 Apr-9 May 2022); a second round (R2) survey (15-27 June 2022 plus additional panellists 8 Sept-16 Oct); a large-group nomenclature consensus meeting (Chicago, IL, USA, July 2022); a third round (R3) survey (17-27 Oct 2022); a second convening (AASLD annual meeting, Washington, DC, USA, Nov 2022) involving both steering committee and larger panel discussions; and, a fourth round (R4) survey (2 Dec 2022-22 Jan 2023) (**Figure 1**). Draft consensus statements contained predominantly 4-point Likert-type response categories related to agreement/disagreement (e.g. agree/somewhat agree/somewhat disagree/disagree), support/opposition, etc., and 3-point responses (e.g., increase, no change, decrease). All statements included a 'not qualified to

respond' option to accommodate the diverse expertise represented in the panel. In addition, in line with established Delphi processes, [11-13] text boxes appeared after panellists entered responses to each statement so they could provide comments and suggest edits, if desired. These were reviewed and used to modify statements in subsequent survey rounds.

Analysis Plan

The survey question and textbox data in the Delphi study required quantitative and qualitative analysis. For the survey question, responses were generated and frequencies for all response categories were recoded to the 4-point response statements to dichotomous construction (e.g., agree + somewhat agree vs. somewhat disagree + disagree) to determine if the level of consensus with individual statements reached the minimum super-majority (i.e. $\geq$67%) cut-off, which was agreed upon *a priori*. For each statement, those selecting 'not qualified to respond' were removed from the denominator to calculate statement frequencies from the relevant sample. The qualitative data collected from the text boxes were reviewed individually by the co-chairs and working group leaders and then discussed in a series of meetings following each survey round to inform decisions regarding statement modification, deletion and/or addition.

For the final decision on both acronym and definition, an external expert committee, comprising content experts from hepatology, endocrinology, paediatrics and patient advocacy representatives, was created and led by two members of the Steering Committee (VR, AJS). The committee was established to represent diversity in terms of expertise and geography, with members chosen based on a prior substantial high-impact publication record in the field. It was composed of 21 members (including 15 who were not part of the Steering Committee) and

included 4 endocrinologists and 5 paediatric hepatologists. The external committee discussed and recommended the final name and acronym from the top three choices that emerged from the final Delphi round. Additionally, based on the output from the Delphi process up to this point, the external committee refined the definition, including metabolic parameters for both adult and paediatric disease. The proposal from this external committee was discussed and approved by the broader NAFLD Nomenclature Steering Committee, and then presented to societies' leadership (AASLD, EASL and ALEH) for additional commentary and approval.

RESULTS

Delphi Panel Characteristics

Invitation to participate on the Delphi panel included seven societies or organisation types, with 29% from EASL, 27% from AASLD, 13% from APASL, 12% from ALEH, 7% from other societies, and 11% from patient advocacy organisations. We collected descriptive information from all Delphi panel participants including demographic and professional data (**Table 1**). The panel was geographically and demographically diverse; panellists from over 50 countries participated with regard to both country of birth (n=59 countries) and country where currently working (n=54 countries). Among the panellists, 40% identified themselves as female and 60% as male. Seventy of the panellists were from the academic sector, with smaller proportions from the public (15%), private (9%), and civil society (3%) sectors. The two largest fields/areas of work were clinical research (54%) and clinical care (28%), with hepatology (82%) accounting for an overwhelming majority of the areas of specialisation. There was substantial NAFLD-related expertise among panellists with 76% indicating they spend 26-100% of their work time in NAFLD-related clinical care, research, or both, and 61% reporting having authored $\geq$21 and 40% had >50 publications on the topic of NAFLD (**Figure 2**).

Response rates and panel participation

The R1 survey consisted of 37 statements within three domains: (1) Nomenclature and distinctions among disease elements (e.g., diagnostic criteria, prognosis, treatment); (2) Other factors possibly influencing consideration of additional or alternative terms; (3) Name/term preferences **(Supplementary Table 1).** Of 236 invited experts in R1, 206 participated and rated these statements (Response rate [RR] = 87%). They also provided 870 comments, which were

reviewed and incorporated as additional statements and a new paediatric focused domain into the second round of consensus statements, with a total of 54 statements. Of the 236 panellists invited for R2, 195 participated in R2 (overall participation, 195+30, RR=83%), providing 1,370 comments. Comments were organised thematically by their content and reviewed by the leads who then proposed modifications to statements if appropriate, eliminated statements if redundant or as suggested by comments, or carried the statements forward to the next round. To minimise survey fatigue, statements thought to be repetitive or ambiguous were removed from the following round. Additionally, statements covering areas of high consensus were not carried forward to R3. Revised statements were shared with the full Steering Committee before proceeding with the next round. For example, in R3, statement revision resulted in 44 statements; there were 187 participants (of 226 invited, RR=83%) who provided an additional 268 comments.

After R2, all Delphi panellists were invited to an in-person (hybrid, i.e. with remote access) 1.5-day nomenclature consensus conference co-hosted by AASLD and EASL in Chicago, IL, USA July 8-9, 2022 for in-depth discussion of the extensive feedback generated from the first two rounds of data collection. This convening provided valuable guidance from a broader group that included the steering committee as well as the broader group of survey panellists to inform statement revision for the third round. The second in-person convening occurred at the annual AASLD conference on 6th November 2022 in Washington DC, USA with two fora for consideration and discussion of the third Delphi round - a closed meeting of the steering committee (n=34 in attendance) followed by a large-group session open to all 2022 AASLD

participants including all Delphi panellists. These discussions provided further clarity on the key elements to include in the final round of the nomenclature consensus process.

Based on this feedback, the R4 survey took panellists through a series of four questions that allowed them to select their first and second choices pertaining to terminology preference, whether the term *metabolic* should be included in the name, the preferred nomenclature (based on their prior choices), and whether or not diagnostic criteria should be revised. Of 224 invited panellists, 174 participated (RR=78%) and provided 28 comments in a final open-ended textbox. **(Supplementary Figure 1)**

Data informing nomenclature considerations (R1-R4+)

Supplementary Table 1 shows the evolution of survey statements across survey rounds 1-3 and the degree of agreement in each round. Statements were modified for clarity, changed or removed based on review of open text comments, and output from face-to-face meetings. The main conclusions emerging by survey rounds are summarised in **Figure 3**. In the 4th Delphi round only 4 questions were asked to clarify remaining points of disagreement. **(Figure 4, Supplementary Figure 1)**

Desire for a name change and the role of stigma

During round 1, a supermajority of respondents (74%) felt that the current names NAFLD and NASH were sufficiently flawed to consider a name change. **(Supplementary Table 1)** The terms 'nonalcoholic' and 'fatty' were deemed to be stigmatising by 61% and 66% of respondents, respectively. A nomenclature that describes the underlying cause of the disease was preferred

by 89% of respondents. While there were concerns over the precise meaning of 'metabolic' and to what extent this term was understood by clinicians, a super-majority felt that having 'metabolic disease or dysfunction' in the name would help patients better understand their disease (72%) and help healthcare professionals better explain or understand the disease (80%). Only a simple majority (56%) felt the terminology of 'metabolic dysregulation' to be a clearly defined clinical entity, although a supermajority (86%) felt that it highlighted a central aspect of disease pathophysiology.

Considerations regarding structure and composition of a new name

When given the choice of whether to select an 'umbrella' term encompassing different disease subcategories, 78% of respondents preferred the idea of an overarching term to encompass the replacement term for NAFLD, ALD and other conditions resulting in hepatic steatosis. Potential overarching terms were informed by survey rounds 2 and 3 and included fatty liver disease, steatotic liver disease, and lipogenic liver disease. Panellists were instructed to rank order their preference, as first, second and third choice. Fatty liver disease, steatotic liver disease, and lipogenic liver disease garnered 46%, 48% and 7% of first choice selections, respectively. When considering the combination of 1st and 2nd choice votes, steatotic liver disease was chosen by 95% of respondents. Sixty-eight % of the panellists preferred the use of a literal name (such as steatotic liver disease) as opposed to using a numerical subtype (such as type 1, type 2, etc.) as part of the new nomenclature. In round 4, 67% of respondents felt that the term 'metabolic' should be included in the revised nomenclature for the alternative name for NAFLD, as a subtype under the overarching term of steatotic liver disease chosen in R3 **(Figure 5)**. Respondents were also asked whether a cardiometabolic risk factor should be added to the

current definition and a simple majority were in favour of adding a metabolic qualifier to the definition.

Considerations for disease definition

Respondents were asked their opinion regarding the concept of steatohepatitis as an important entity, and 95% of respondents felt the presence of steatohepatitis had prognostic implications and should remain an important distinction. Additionally, given the role of 'resolution of steatohepatitis' as one of the two European Medicines Agency (EMA) and US Food and Drug Administration (FDA) approvable endpoints, 93% felt it should remain for both clinical practice and trial endpoints.[14, 15] The current definition of NAFLD excludes consumption of >20g/30g of alcohol per day in females and males, respectively, with a more liberal approach to concomitant alcohol use proposed in the original MAFLD definition.[5, 7] To establish the permissibility of greater alcohol consumption, several questions were asked to better understand the impact of alcohol on the natural history of the disease and also how to characterise various levels of alcohol use in the definition. A supermajority felt that consumption of 30g-60g of alcohol daily in the setting of NAFLD alters the natural history of disease (95%) and may alter response to therapeutic interventions (90%). Furthermore, 90% felt that individuals with steatosis related to metabolic risk factors who consume more than minimal alcohol (30g-60g daily) represented an important group that should be considered in a different disease category and studied independently.

Perceived impact of name and/or definition change on disease awareness, development of biomarkers or clinical trials

When considering the potential impact of a change in name, definition or both, fifty-six percent felt that a change in nomenclature would positively impact disease awareness. In assessing the impact of a change in name only on the interpretation of existing and emerging clinical trial results, 18%, 72% and 11% **(Supplementary Table 1; R3, Statement 27)** felt it would hinder, have no impact and enhance, respectively. When a similar question was asked about the impact on regulatory approval of biomarkers if the name but not the definition changes, 12%, 63% and 25% felt it would accelerate, have no impact or delay approval respectively. In the event of both a name and definition change, 60% of respondents were concerned this could hinder the interpretation of existing and emerging clinical trial results that used the currently accepted definition of NAFLD, whereas 20% felt it would enhance and 20% thought there would be no impact. A simple majority (59%) felt that a change in disease definition would likely delay regulatory approval of biomarkers (R3 – S24) whereas 63% felt a change in name only would have no effect. Of note these questions did not discuss the proposed change to the definition.

Paediatric perspective

There was a high degree of consensus among the paediatric panellists when considering statements/questions pertaining to the paediatric population. Only paediatricians answered the paediatrics specific questions, and the main themes addressed the role of stigma, use of the term 'metabolic' and the histological definition of the disease. In children and adolescents, 60% felt that use of the term 'nonalcoholic' was stigmatising for parents and/or paediatric patients, with 55% finding this to be the case with the term 'fatty'. When asked if the current definition

of NASH is less useful in children and adolescents due to a lower frequency of hepatocyte ballooning, 95% agreed that a reassessment of the definitions of steatohepatitis in the paediatric setting would be beneficial. In considering incorporation of the term 'metabolic' into the nomenclature, 90% estimated that this term may be confusing in the paediatric context since inborn errors of metabolism are referred to as 'metabolic liver disease'.

Proposed new nomenclature for NAFLD, NASH and NAFLD with increased alcohol consumption

When considering different subcategories under the overarching term of SLD, 67% of respondents preferred the NAFLD replacement term to include the word 'metabolic'. The top 3 acronyms, metabolic dysfunction-associated steatotic liver disease (MASLD), MetSLD, or metabolic steatotic liver disease (MSLD) were 30%, 30% and 22%, respectively **(Figure 4)**. In total, 75% of respondents of the external expert committee chose metabolic dysfunction-associated steatotic liver disease (MASLD) as the replacement term for NAFLD and 88% metabolic dysfunction-associated steatohepatitis (MASH) as the replacement term for NASH. The acronym MetALD was chosen by 28% and MAASLD by 33% to represent a separate group of patients with MASLD that consume 140-350 g/week for females and 210-420 g/week for males. MetALD was chosen to avoid the possible confusion or perception associated with the acronym AASLD within MAASLD that may link the acronym to a specific professional association. Within MetALD there is a continuum where conceptually the condition can be seen to be MASLD or ALD predominant. This may vary over time within a given individual.

Proposed modifications to current definition

The strong epidemiological and pathogenic link between NAFLD, metabolic dysfunction and insulin resistance, informed a view in the external expert committee that the diagnosis be based on affirmative rather than exclusionary criteria such as nonalcoholic. There was near universal agreement that the criteria be defined sufficiently broadly to identify both individuals with obesity and cardiometabolic risk factors in the context of regional/ethnic differences. Simple, readily available and easily measurable parameters were also deemed necessary for this set of criteria to be broadly applied in clinical practice and in various clinical settings. Finally, the diagnostic criteria were selected to align with cardiometabolic risk factors believed to be associated with insulin resistance and already well-established and validated in the context of cardiovascular disease. [16] It was agreed that patients with steatosis and any one of the cardiometabolic criteria outlined in **Figure 6** would be considered to have MASLD. Of note, making a diagnosis of MASLD does not imply that other causes of SLD do not need to be considered, which is particularly relevant in children where it is imperative to exclude other causes of hepatic steatosis prior to applying the MASLD diagnostic criteria to ensure that dual pathology is not missed.[17]

Switching from a definition based on the exclusion of any other liver disease (i. e. NAFLD) to a definition based on specific, primarily cardiometabolic risk factors (i. e. MASLD) has potential limitations. Firstly, the key metabolic dysfunction underlying MASLD is insulin resistance, and the selected metabolic risk factors do not equally predict insulin resistance, as for example diastolic blood pressure and HDL-C are only weakly associated with insulin resistance.[18]

Secondly, insulin resistance and steatosis may be present in the absence of any cardiometabolic risk factors, especially in younger adults in the primary care setting. Thus, patients with steatosis without overt cardiometabolic risk factors or other discernible cause are labelled as cryptogenic. If there is uncertainty and the clinician strongly suspects metabolic dysfunction despite the absence of CMRF then the term possible MASLD can be considered pending additional testing (e.g., HOMA-IR, OGTT) although this should be left to the discretion of the clinical team. Such cases and also cryptogenic cases that subsequently manifest CMRF can be rebadged as MASLD.

Role of alcohol in disease definitions

With respect to alcohol intake, the overwhelming consensus was to continue to limit alcohol intake (as previously limited for NAFLD) in the context of steatosis. The purpose of this process was to focus on NAFLD, not alcohol-related liver disease, but it was seen as relevant to comment on situations where these was overlap. We therefore created a separate category outside of pure MASLD, namely MetALD, with alcohol intake greater than that allowed for NAFLD/MASLD. Within the group of patients with MetALD, there may be individuals where MASLD is the perceived dominant driver and others where ALD is the perceived dominant driver, and indeed this may change over time. **(Figure 5).**

Discussion

Identification of a new name and definition for the condition formerly known as nonalcoholic fatty liver disease has been a challenging process given the broad range of global stakeholders. It is imperative that any new proposal be sufficiently better than the existing nomenclature and that it enhances awareness, understanding of the disease and drug/biomarker development. This robust, representative, patient-centric Delphi process systematically addressed all the issues and views over the past years and through consensus has arrived at both a new name and a refined definition. By inclusion of patient advocacy groups throughout the entire process, the new nomenclature strives to accelerate disease awareness whilst minimising stigma associated with use of terms perceived as stigmatising by some patients and their caregivers.

Several important findings emerged from the nomenclature consensus process; there was clear support for a name change, use of an overarching term which could accommodate the evolution of disease understanding, and use of a metabolic descriptor in the new nomenclature. Both the overarching term of steatotic liver disease (SLD) and the more specific metabolic dysfunction-associated steatotic liver disease (MASLD) provide an affirmative non-stigmatising description of the condition rather than a diagnosis of exclusion. This is also seen in the definition, which requires the presence of at least one cardiometabolic risk factor in addition to hepatic steatosis. The proposed nomenclature is not intended to be static, but rather allows the flexibility for refinement as new evidence emerges about underlying pathophysiology and risk factors.

A key consideration is the preservation of existing data on natural history, biomarkers and clinical trials as part of these changes. To address the impact of the refined definition, an analysis of the LITMUS consortium European was performed, which demonstrated that 98% of the existing Registry cohort of patients with NAFLD would fulfill the new criteria for MASLD.[19] Conceptually patients with the previous definition (NAFLD) can now be seen to be completely covered by the categories of MASLD and possible MASLD. The introduction of a separate MetALD subcategory where metabolic and alcohol-related risk factors coexist sits outside MASLD/NAFLD and is an opportunity to generate new knowledge for this common group of patients. In addition, maintenance of the term, and clinical definition, of steatohepatitis ensures retention and validity of prior data from clinical trials and biomarker discovery studies of patients with NASH to be generalizable to individuals classified as MASLD or MASH under the new nomenclature, without impeding the efficiency of research.

The Delphi process utilised a super-majority threshold of ≥67% with two exceptions, the consideration of stigma and a binary question to retain or revise the current definition. Whilst recognizing that perceptions of stigma differ widely,[20, 21] especially across different languages and cultures, in this study it became clear that substantial proportions of the respondents deemed terms such as ‘fatty’ stigmatising, hence its exclusion as part of any new name. Although health care professionals may contend that patients have not reported this previously, this likely reflects in part a failure to ask the question in the first place and the power imbalance in the doctor-patient relationship. Moreover, a recent large study indicated that some health care professionals and patients considered the terms fatty and nonalcoholic

to be pejorative and stigmatising.[21] The use of medical terminology such as steatosis may at one level be seen as over-medicalising the lexicon yet it affords patients the opportunity to disclose their condition to friends and colleagues without having to face prejudice and stigma that can be inherent to the word 'fatty'.[21, 22] Efforts to increase disease awareness have had modest success, possibly impacted by the perception that care providers deem the term 'fatty liver' as describing an indolent condition. With therapeutics on the horizon, there is renewed energy to identify 'at-risk' patients, which in conjunction with new terminology may bolster awareness and sense of importance.

The overarching term of steatotic liver disease encompasses the spectrum of causes of hepatic steatosis, thus allowing precise classification once a specific aetiology has been identified. The new names also allow for further characterization of fibrotic severity, e.g. MASH with stage 3 fibrosis. Disease staging and severity are not altered by this process, although it is anticipated that in the near to medium term, disease staging will be achieved using non-invasive tests, which can be incorporated into further clarifications of disease stage. Thus, the current consensus process does not deviate from prior case definitions for steatohepatitis and disease stages.[23] The diagnosis of MASLD/MASH with advanced fibrosis cirrhosis, when steatosis may not be present, will be based upon existing agreed criteria for NASH cirrhosis.[23] This also applies to patients with MetALD and ALD with significant fibrosis who may not have steatosis, yet have SLD as part of the over-arching nomenclature, reflecting the mechanism of injury.

The proposed nomenclature also improves upon the prior "nonalcoholic" label and appropriately assigns a metabolic basis for this liver disease which was long recognized as "the

hepatic manifestation of the metabolic syndrome".[5] This important conceptual change has several practical consequences. First, when addressing patients, it allows for a coherent and straightforward explanation of the disease as it is intuitively easier to understand in the context of its underlying cardiometabolic abnormalities linked to insulin resistance and its association with the patient's other conditions, rather than in the framework of a diagnosis of exclusion. This also helps to communicate to the patient the main therapeutic actions to be taken both from a liver and a holistic perspective. Secondly, we believe that using this classification will enhance disease awareness, since the alignment of the diagnostic criteria for MASLD with widely recognized phenotypic traits in diabetes and cardiovascular medicine will make it easier for the larger community of healthcare providers to identify individuals with this condition. There is a strong convergence between the metabolic set of criteria we propose for diagnosing MASLD and those proposed by Eslam *et al*. for MAFLD. [24] However, the current consensus approach decided to prioritise robust and easily accessible clinical criteria and biological measurements, and as such these criteria do not include direct measurements of insulin resistance (such as fasting insulin or HOMA-IR) because of their complexity, cost and variability between laboratories. However, in patients with hepatic steatosis in the absence of overt cardiometabolic risk factors, secondary testing for insulin resistance may be useful to identify those with possible MASLD. It is important to understand that the set of diagnostic criteria for MASLD are not intended to diagnose "metabolic syndrome" or predict the occurrence of cardiovascular outcomes. The cardiometabolic risk factors are intended to identify patients likely to have insulin resistance as the main cause of hepatic steatosis. There was consideration of providing differential weighting for the cardiometabolic risk factors such as type 2 diabetes

although the literature is conflicting in that regard with some indicating no parameter is better than another at identifying hepatic steatosis.[25]

This process focusses on nomenclature and definition of NAFLD rather than a determination of what constitutes hepatic steatosis or assessment of disease severity. There is an extensive literature on the confirmation of hepatic steatosis [26, 27] which we did not seek to interrogate – often this is a pragmatic determination in clinical practice which is where this guidance starts. Moreover, this nomenclature process, in line with published guidance,[21, 28, 29] is not advocating for the routine use of tests to confirm hepatic steatosis although in reality most, if not all, patients will usually have imaging at some point. Finally, we recognise it is the evaluation of fibrosis either as part of screening strategies or individual clinical decisions, which is relevant for most clinical settings.[30] That remains unchanged after this process, other than the name (e.g. MASLD with advanced fibrosis).

Contrary to the initial proposal by Eslam *et al*, the Delphi process revealed that most experts consider that MetALD patients should be classified in a category distinct from MASLD, mainly because of the added pathogenic value of alcohol consumption and consequential prognostic implications. The condition MetALD provides an opportunity to better define the natural history for such patients and the development of biomarkers and therapies which are currently lacking for this group of patients.[31] ALD is a distinct liver disease (of which steatosis is one of the features) and thus categorised under the SLD umbrella. This should raise awareness of alcohol as a driver of steatosis and highlight the impact of excessive alcohol consumption (i.e., higher than 50-60 g daily in females and males, respectively) irrespective of their association with

metabolic dysfunction. Studies have shown that even in excessive drinkers, obesity increases the prevalence of cirrhosis and glycaemic dysregulation increases fibrosis severity.[32, 33] Patterns of alcohol use must also be taken into consideration as bingeing (even within the total weekly 'allowable limit' for MASLD) can be detrimental. We also recognise that validated objective tools are not currently available to determine the relative contribution of MASLD and ALD in patients with MetALD and hence we rely on self-reported alcohol intake which can be inaccurate. In that regard this is a conceptual construct and might be better seen as a disease spectrum with different weights of different modifiable disease drivers (cardiometabolic factors and alcohol). This is also relevant for the distinction between patients with MetALD and those drinking more heavily that are termed as having ALD. Also the category of ALD without metabolic factors is relatively rare amongst patients with significant fibrosis but it was felt to represent part of the spectrum.

In addition to defining a distinct category for patients with MASLD and greater alcohol consumption (MetALD), the proposed nomenclature allows, by introducing the umbrella term of steatotic liver disease, for diagnostic subgroups of steatotic liver disease to be identified, namely those that are drug-related as well as others. The latter encompasses the many "secondary" causes of NAFLD, most of which are rare diseases, including monogenic diseases.[31] This is particularly relevant in children, in whom rare genetic metabolism defects can cause steatosis and must be considered.[17] Patients with steatosis without overt cardiometabolic risk factors or other discernible cause are labelled as cryptogenic, although depending on clinical judgement could also be deemed to have possible MASLD and would benefit from periodic reassessment on a case-by-case basis. Of note, genetic variants

influencing the prevalence and/or severity of MASLD such as *PNPLA3*, *TM6SF2* and *HSD17B13*, and other genetic risk variants that are common in the general population, were not considered a distinct nosological entity. This was because these variants are disease modifiers for both MASLD and ALD rather than causative factors, in contrast to rare variants responsible for monogenic diseases. The change in nomenclature in favour of a positive diagnosis based on the presence of cardiometabolic risk factors will also allow for a rational reclassification of most cases of the condition formerly known as "lean NASH" into the regular MASLD category, as long as currently defined metabolic risk factors are present. The "cryptogenic" category will, as mentioned, also accommodate the rare specific causes of steatotic liver disease unrelated to metabolic dysfunction, alcohol consumption, drug intake or other causes [34] while waiting for a precise identification of the causal agent by future research.

Despite the many strengths of this rigorous process, we acknowledge limitations. The individual statements changed between R1 and R3 (Supplementary Table 1) and there was variation in levels of agreement for individual statements although this reflects their evolution, as important issues arose that we needed to consider regarding the NAFLD nomenclature. Furthermore, the lack of uniform agreement on many topics reflects the diversity of opinions involved in the process. *A priori*, we chose a threshold of 67% (supermajority) to define consensus, which meant that some opinions, although held by a simple majority (more than 50% but less than 67%), did not influence the final decisions, with the exception of stigma and the decision to alter the disease definition. Nonetheless, we are confident that statements supported by a super majority were addressed and incorporated.

In conclusion, we believe this process, which has multi-stakeholder endorsement, provides a strong platform from which we can increase disease awareness, reduce stigma and accelerate drug and biomarker development for the benefit of patients with MASLD, MASH and MetALD.

Acknowledgements

The authors would like to express their appreciation to the governing boards of the three lead societies AASLD, ALEH and EASL, and specifically society leadership, Norah Terrault (AASLD President 2023), Laurie DeLeve (AASLD President 2022), and W. Ray Kim (AASLD President-elect); Graciela Castro Narro (ALEH President); Thomas Berg (EASL Secretary General 2021-2023) and Aleksander Krag (EASL Secretary General 2023-2025). The authors would also like to thank Matthew D'Uva from AASLD for his tireless work and support of this project and recognize the contributions of all of the members of the NAFLD nomenclature consensus group who provided feedback, analysis, and recommendations over multiple Delphi rounds. (Table 2) We acknowledge the assistance of the EU - IMI2 funded LITMUS (Liver Investigation: Testing Marker Utility in Steatohepatitis) consortium for analysis of data derived from the European NAFLD Registry. Finally, the authors and methodology team would also like to thank Delfina Boudou and Trenton White (ISGlobal, Spain).

References

1. Ludwig, J., et al., *Nonalcoholic steatohepatitis: Mayo Clinic experiences with a hitherto unnamed disease.* Mayo Clin Proc, 1980. **55**(7): p. 434-8.
2. Kleiner, D.E., et al., *Design and validation of a histological scoring system for nonalcoholic fatty liver disease.* Hepatology, 2005. **41**(6): p. 1313-21.
3. Brunt, E.M., *Nonalcoholic steatohepatitis (NASH): further expansion of this clinical entity?* Liver, 1999. **19**(4): p. 263-4.
4. Bedossa, P., et al., *Histopathological algorithm and scoring system for evaluation of liver lesions in morbidly obese patients.* Hepatology, 2012. **56**(5): p. 1751-9.
5. Matteoni, C.A., et al., *Nonalcoholic fatty liver disease: a spectrum of clinical and pathological severity.* Gastroenterology, 1999. **116**(6): p. 1413-9.
6. Eslam, M., et al., *MAFLD: A Consensus-Driven Proposed Nomenclature for Metabolic Associated Fatty Liver Disease.* Gastroenterology, 2020. **158**(7): p. 1999-2014 e1.
7. Eslam, M., et al., *A new definition for metabolic dysfunction-associated fatty liver disease: An international expert consensus statement.* J Hepatol, 2020. **73**(1): p. 202-209.
8. Eslam, M., et al., *The Asian Pacific Association for the Study of the Liver clinical practice guidelines for the diagnosis and management of metabolic associated fatty liver disease.* Hepatol Int, 2020. **14**(6): p. 889-919.
9. Younossi, Z.M., et al., *From NAFLD to MAFLD: Implications of a Premature Change in Terminology.* Hepatology, 2021. **73**(3): p. 1194-1198.
10. Ratziu, V., et al., *The times they are a-changin' (for NAFLD as well).* J Hepatol, 2020. **73**(6): p. 1307-1309.
11. Beiderbeck, D., et al., *Preparing, conducting, and analyzing Delphi surveys: Cross-disciplinary practices, new directions, and advancements.* MethodsX, 2021. **8**: p. 101401.
12. Trevelyan, E.G., W.A. Turner, and N. Robinson, *Developing an acupuncture protocol for treating phantom limb pain: a Delphi consensus study.* Acupunct Med, 2015. **33**(1): p. 42-50.
13. M, L.H.a.T., *The Delphi Method: Techniques and Applications*. 2002, Portland: Portland State University.
14. Rinella, M.E., et al., *Report on the AASLD/EASL Joint Workshop on Clinical Trial Endpoints in NAFLD.* Hepatology, 2019. **70**(4): p. 1424-1436.
15. Loomba, R., et al., *Expert Panel Review to Compare FDA and EMA Guidance on Drug Development and Endpoints in Nonalcoholic Steatohepatitis.* Gastroenterology, 2022. **162**(3): p. 680-688.
16. Alberti, K.G., et al., *Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity.* Circulation, 2009. **120**(16): p. 1640-5.
17. European Society for Paediatric Gastroenterology, H., et al., *Diagnosis of fatty liver in children should occur in parallel to investigation for other causes of liver disease.* Lancet Gastroenterol Hepatol, 2023.

18. Carr, D.B., et al., *Intra-abdominal fat is a major determinant of the National Cholesterol Education Program Adult Treatment Panel III criteria for the metabolic syndrome.* Diabetes, 2004. **53**(8): p. 2087-94.
19. Hardy, T., et al., *The European NAFLD Registry: A real-world longitudinal cohort study of nonalcoholic fatty liver disease.* Contemp Clin Trials, 2020. **98**: p. 106175.
20. Karlsen, T.H., et al., *The EASL-Lancet Liver Commission: protecting the next generation of Europeans against liver disease complications and premature mortality.* Lancet, 2022. **399**(10319): p. 61-116.
21. Zobair M. Younossi, Y.Y., Jian-Gao Fan, Vincent Wai-Sun Wong, Mohammed El-Kassas, Shira Zelber-Sagi, Alina M. Allen, Mary Rinella, Ahwani K. Singal, Stuart Gordon, Michael Fuchs, Wayne Eskridge, Naim Alkhouri, Khaled Alsawat, Hirokazu Takahashi, Takumi Kawaguchi, Jane Ranagan, Ming-Hua Zheng, Ajay Duseja, Patrizia Burra, Patrizia Carrieri, Marco Arrese, Achim Kautz, Janus P. Ong, Laurent Castera, Sven Francque, Marcelo Kugelmas, Yuichiro Eguchi, Sombat Treeprasertsuk, Marlen I. Castellanos Fernández, Manuel Romero-Gómez, Phil Newsome, Kenneth Cusi, Rohit Loomba, Jörn M. Schattenberg, Ming Lung Yu, Moises Diago, Lynn Gerber, Brian Lam, Lisa Fornaresio, Fatema Nader, Linda Henry, Andrei Racila, Pegah Golabi, Maria Stepanova, Saleh A. AlQahtani, Jeffrey V. Lazarus and the Global NASH Council, *Stigma in NAFLD and NASH: A Global Survey of Patients and Providers.* Hepatology, 2023.
22. Carrieri, P., et al., *Knowledge of liver fibrosis stage among adults with NAFLD/NASH improves adherence to lifestyle changes.* Liver Int, 2022. **42**(5): p. 984-994.
23. Siddiqui, M.S., et al., *Case definitions for inclusion and analysis of endpoints in clinical trials for nonalcoholic steatohepatitis through the lens of regulatory science.* Hepatology, 2018. **67**(5): p. 2001-2012.
24. Eslam, M. and J. George, *Reply to: correspondence regarding "A new definition for metabolic dysfunction-associated fatty liver disease: An international expert consensus statement": Bringing evidence to the NAFLD-MAFLD debate.* J Hepatol, 2020. **73**(6): p. 1575.
25. Wong, V.W., et al., *Prevalence of non-alcoholic fatty liver disease and advanced fibrosis in Hong Kong Chinese: a population study using proton-magnetic resonance spectroscopy and transient elastography.* Gut, 2012. **61**(3): p. 409-15.
26. Petroff, D., et al., *Assessment of hepatic steatosis by controlled attenuation parameter using the M and XL probes: an individual patient data meta-analysis.* Lancet Gastroenterol Hepatol, 2021. **6**(3): p. 185-198.
27. Eddowes, P.J., 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**(6): p. 1717-1730.
28. Rinella, M.E., et al., *AASLD Practice Guidance on the clinical assessment and management of nonalcoholic fatty liver disease.* Hepatology, 2023. **77**(5): p. 1797-1835.
29. European Association for the Study of the Liver. Electronic address, e.e.e., et al., *EASL Clinical Practice Guidelines on non-invasive tests for evaluation of liver disease severity and prognosis - 2021 update.* J Hepatol, 2021. **75**(3): p. 659-689.

30. Taylor, R.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**(6): p. 1611-1625 e12.
31. Moreno, C., et al., *"Dual aetiology fatty liver disease": A recently proposed term associated with potential pitfalls.* J Hepatol, 2021. **74**(4): p. 979-982.
32. Naveau, S., et al., *Excess weight risk factor for alcoholic liver disease.* Hepatology, 1997. **25**(1): p. 108-11.
33. Raynard, B., et al., *Risk factors of fibrosis in alcohol-induced liver disease.* Hepatology, 2002. **35**(3): p. 635-8.
34. Liebe, R., et al., *Diagnosis and management of secondary causes of steatohepatitis.* J Hepatol, 2021. **74**(6): p. 1455-1471.

Figures Legends

Figure 1-Summary of the Delphi Process

The *top section* depicts the iterative sampling approach employed to generate a large, diverse Delphi panel (267 experts *invited* and 225 *participated* across the four rounds). The two co-chairs, from AASLD and EASL, respectively, convened representatives from several other large pan-national societies and patient advocacy organizations to form the Steering Committee. This group identified six topics/working groups that led the development of a preliminary set of consensus statements, which were reviewed by the larger steering committee and subsequently revised. The co-chairs elicited nominations for Delphi panel members from a diverse group of liver organizations. The *bottom section* depicts the four survey rounds (R1-R4) of data collection from the full Delphi panel, which involved panelists' indicating their level of agreement/disagreement (i.e., consensus) with statements in each survey round, as well as the ability to provide comments in open-ended text boxes. Draft consensus statements were revised based on panelists' comments for subsequent rounds. Two large expert convenings were held following R2 and R3 to permit group discussion of issues raised from the survey data collection components of the Delphi methodology. RR = response rate.

Figure 2 NAFLD-Related Professional Characteristics of Delphi Panelists

NAFLD = nonalcoholic fatty liver disease.

Data in panel A represent the number of respondents (x axis) and percentage (y axis) of time spent in NAFLD-related clinical care, research or both. Similarly, panel B depicts the number of respondents (x axis) and percentage (y axis) that have (co)authored articles on the topic of NAFLD.

Figure 3 Overview of main findings by Delphi round

The conclusions reached at the end of each Delphi round are depicted here. Results are shown at each corresponding Delphi round with respect to name change and definition, depicted in light green and orange, respectively. An independent subcommittee comprised of expert endocrinologists, hepatologists, pediatricians and patients chose between the top 3 acronyms emerging from the 4th Delphi round and outlined the specifics of the definition to include cardiometabolic parameters, as dictated by the 4th Delphi round.

Figure 4 NAFLD Nomenclature Result: Round 4 (Summary)

Delphi round 4 consisted of 4 questions. All respondents responded to all questions irrespective of their response to the preceding question. These are the aggregate results for respondents on each question. The first question addressed whether a literal term to replace NAFLD was preferred over a numerical subtype (e.g. Type 1,2,3 etc.) and 68% preferred the literal term. The

second was whether or not the term 'metabolic' should be included in the name and 67% felt it should. The third presented a choice of acronyms that had emerged as the top 4 in Delphi R3 and the top 3 (nearly equal in preference) were advanced to the expert panel for a final decision as there was no clear majority. The last question was binary and simply asked if the definition of the NAFLD replacement term should be retained or refined to include a cardiometabolic qualifier.

Figure 5 Steatotic Liver Disease sub-classification

This depicts the schema for Steatotic Liver Disease (SLD) and its sub-categories. SLD, diagnosed histologically or by imaging, has many potential etiologies. MASLD, defined as the presence of hepatic steatosis in conjunction with one CMRF and no other discernible cause, ALD, and an overlap of the 2 (MetALD), comprise the most common causes of SLD. Within the MetALD group there exists a continuum across which the contribution of MASLD and ALD will vary. To align with current literature, limits have been set accordingly for weekly and daily consumption, understanding that the impact of varying levels of alcohol intake are evolving. Other causes of SLD need be considered separately, as is already done in clinical practice, given their distinct pathophysiology. Multiple etiologies of steatosis can coexist. If there is uncertainty and the clinician strongly suspects metabolic dysfunction despite the absence of CMRF then the term possible MASLD can be considered pending additional testing (e.g., HOMA-IR, OGTT). Those with no identifiable cause (cryptogenic SLD) may be recategorised in the future pending developments in our understanding of disease pathophysiology. Lastly, the ability to provide an affirmative diagnosis allows for the coexistence of other forms of liver disease with MASLD, e.g. MASLD + autoimmune hepatitis or viral hepatitis.

Figure 6 MASLD diagnostic criteria

In the presence of hepatic steatosis, the finding of any of a cardiometabolic risk factor, would confer a diagnosis of MASLD if there are no other causes of hepatic steatosis. If additional drivers of steatosis are identified, then this is consistent with a combination etiology. In the case of alcohol this is termed MetALD. In the absence of overt cardiometabolic criteria, other etiologies must be excluded and if none is identified, this is termed cryptogenic SLD, although depending on clinical judgment could also be deemed to
be possible MASLD and thus would benefit from periodic reassessment on a case-by-case basis.

Supplementary Figure 1. NAFLD Nomenclature Result: Round 4 (Complete)

The fourth and final Delphi round to achieve consensus on a nomenclature was informed by the results from the previous three Delphi rounds (see **Table 2**) as well as feedback from multiple in-person convenings involving in-depth discussion among panel members. Thus, round 4 comprised a series of questions depicted in the flow chart above that enabled panel members to select both their preferred/first-choice nomenclature as well, as their preference should an option other than their first-choice garner majority support from the panel. The results of this process are presented in this figure.

Legend: Q displayed to all; Q displayed if person chose A/numerical in Q1; Q displayed if person chose B/literal in Q1; Q displayed if person chose A/incl 'Metabolic' in Q2b or Q2b1; Q displayed if person chose B/does not incl Metabolic in Q2b or Q2b1.

Abbreviations: NAFLD, non-alcoholic fatty liver disease; Q, question; SLD, steatotic liver disease; incl, include; *MetSLD, metabolic dysfunction- associated steatotic liver disease; *MSLD, metabolic dysfunction-associated steatotic liver disease; MAS, metabolic dysfunction- associated steatosis; MHS, metabolic dysfunction-associated hepatic steatosis; *MASLD, metabolic dysfunction-associated steatotic liver disease; VASLD, visceral adiposity-associated steatotic liver disease; LLD, lipotoxic liver disease; NASLD, nutrition-associated steatotic liver disease; IRSLD, insulin-resistance associated steatotic liver disease.

*Note: These names appear to be the same but each has distinct characteristics; refer to survey Q3a or Q3b1 for details.

Table 1. Delphi Panel Characteristics (N=225)

	N	%
Professional characteristics		
Primary sector of employment		
Civil society	7	3
Private	21	9
Public	34	15
Academic	158	70
Other	4	2
Primary field/area of work		
Clinical research	118	54
Healthcare provider	61	28
Non-clinical research	13	6
Patient/policy advocacy	18	9
Other	7	4
Primary area of specialty/expertise* (among healthcare providers, clinical and non-clinical researchers)		
Gastroenterology	7	4
Endocrinology	13	7
Hepatology	151	82
Other	13	8
Years working in the field post-training		
0-12	53	29
13-24	69	37
25-36	51	27
37-48	13	7
% of work in NAFLD-related clinical care, research or both		
0-25	26	12
26-50	61	27
51-75	68	30
76-100	44	19
Number of articles (co)authored on topic of NAFLD		
<6	32	17
6-20	42	22
21-50	39	21
>50	74	40
Liver organization associated with *(N invited)*		
AASLD *(72)*	60	27
ALEH *(30)*	27	12
APASL, AMAGE, INASL, SAASL, TASL *(41)*	29	13
EASL *(70)*	66	29
GI and endocrinological societies *(21)*	15	7
Pathology societies *(4)*	3	1
Patient organization *(29)*	24	11

Personal Characteristics		
Gender		
Woman	88	40
Man	135	60
Non-binary or gender diverse	0	0
Prefer not to say	0	0
Country where born (N=59)[+]		
High income	163	73
Low and middle income	61	27
Country where currently working (N=54)[+]		
High income	183	82
Low and middle income	41	18

Notes: Ns for different characteristics vary due to missing data; percentages may not sum to 100 due to rounding. With respect to respondent area of expertise 184 of 192 participating healthcare providers and researchers responded to the request to provide their area of expertise. *24 panelists indicated that in their clinical practice or liver-focused research, they routinely care for or focus on liver disease patients who are under 18 years old. Note that numbers represent those that engaged in the process, rather than those who were invited to join the process, but did not respond. [+]N of total countries represented.

Abbreviations: AASLD, American Association for the Study of Liver Disease; ALEH, Asociación Latinoamericana para el Estudio del Hígado (Latin American Association for the Study of the Liver); AMAGE, African Middle East Association of Gastroenterology; APASL, Asian Pacific Association for the Study of the Liver; EASL, European Association for the Study of the Liver; GI, gastrointestinal; INASL, Indian National Association for the Study of the Liver; NAFLD, non-alcoholic fatty liver disease; SAASL, South Asian Association for Study of the Liver; TASL, Taiwan Association for the Study of the Liver.

Table 2

NAFLD Nomenclature Consensus Group

Recipient First Name	Recipient Last Name	Country
Manal	Abdelmalek	United States
Leon	Adams	Australia
Veeral	Ajmera	United States
Mamun	Al Mahtab	Bangladesh
William	Alazawi	United Kingdom
Maryam	Alkhatry	United Arab Emirates
Naim	Alkhouri	United States
Alina	Allen	United States
Michael	Allison	United Kingdom
Khalid	Alswat	Saudi Arabia
Michele	Alves-Bezerra	United States
Quentin	Anstee	United Kingdom
Juan Pablo	Arab	Canada
Matthew J.	Armstrong	United Kingdom
Marco	Arrese	Chile
Diego	Arufe	Argentina
Pablo	Aschner	Colombia
Amon	Asgharpour	United States
Gyorgy	Baffy	United States
Maya	Balakrishnan	United States
Meena	Bansal	United States
Pierre	Bedossa	United States
Cynthia	Behling	United States
Renata	Belfort	United States
Carlos	Benítez	Chile
Thomas	Berg	Germany
Annalisa	Berzigotti	Germany
Michael	Betel	United States
Ulrich	Beuers	Netherlands
Cristiana	Bianco	Italy
Jerome	Boursier	France
Clifford	Brass	United States
Carol L.	Brosgart	United States
Elizabeth Matthews	Brunt	United States
Elisabetta	Bugianesi	Italy
Maria	Buti	Spain
Christopher	Byrne	United Kingdom
Steve	Caldwell	United States
Rotonya	Carr	United States
Teresa	Casanovas	Spain
Marlene	Castellanos-Fernández	Cuba

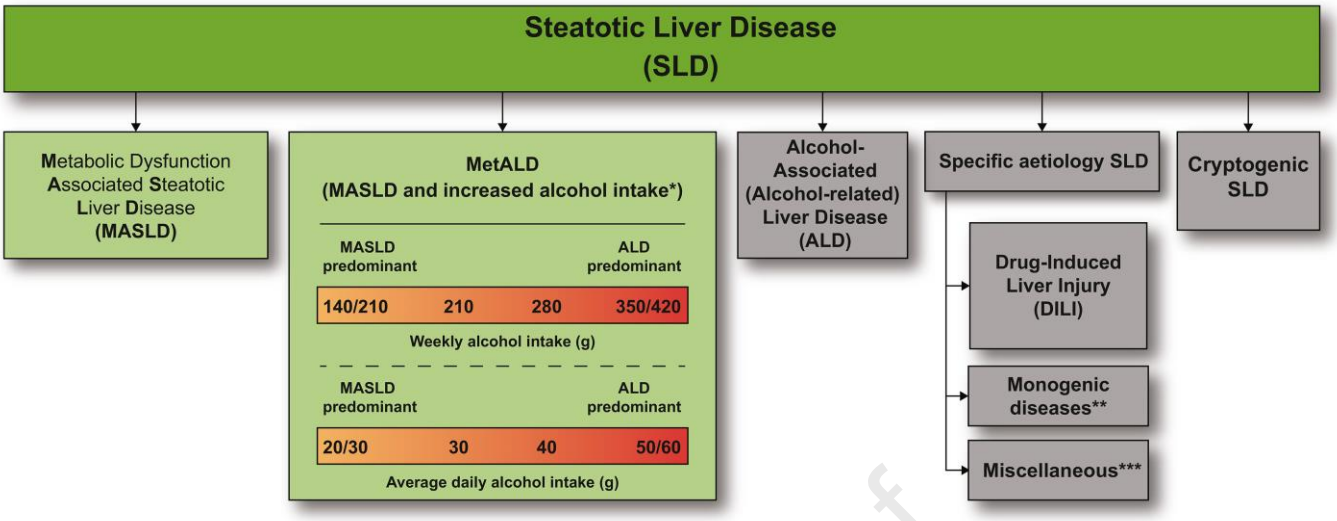
Laurent	Castera	France
Graciela	Castro-Narro	México
Cyrielle	Caussy	France
Eira	Cerda	México
Naga	Chalasani	United States
Wah Kheong	Chan	Malaysia
Phunchai	Charatcharoenwitthaya	Thailand
Michael	Charlton	United States
Amanda	Cheung	United States
Daniela	Chiodi	Argentina
Ray	Chung	United States
David	Cohen	United States
Kathleen	Corey	United States
Helena	Cortez-Pinto	Portugal
Helma P.	Cotrim	Brazil
Javier	Crespo	Spain
Deborah	Crosby	United States
Donna	Cryer	United States
Kenneth	Cusi	United States
Yock Young	Dan	Singapore
Anuradha	Dassanayake	Sri Lanka
Nicholas	Davidson	United States
Robert	De Knegt	Netherlands
Victor	De Ledinghen	France
Münevver	Demir	Germany
Moutaz	Derbala	Qatar
Sebastian	Diaz	Colombia
Anna Mae	Diehl	United States
Bruce	Dimmig	United States
Melisa	Dirchwolf	Argentina
Ajay	Duseja	India
Karel	Dvorak	Prague
Mattias	Ekstedt	Sweden
Reda	El Wakil	Egypt
Mohammed	El-Kassas	Egypt
Wayne	Eskridge	United States
Jiangao	Fan	China
Geoffrey	Farrell	Australia
María Lucía	Ferraz	Brazil
Yasser	Fouad	Egypt
Sven	Francque	Belgium
Dave	Frank	United States
Scott	Friedman	United States
Angie	Fry Carpenter	United States
Michael	Fuchs	United States
Rino	Gani	Indonesia

Amalia	Gastaldelli	Italy
Anja	Geerts	Belgium
Andreas	Geier	Germany
Marcos	Girala	Paraguay
George	Goh	Singapore
Nicolas	Goossens	Switzerland
Cheryl	Grainger	United States
Isabel	Graupera	Catalonia
Cynthia	Guy	United States
Hannes	Hagström	Sweden
Stephen	Harrison	United States
Zachary	Henry	United States
Bela	Hunyady	Hungary
Alan	Hutchison	United States
Scott	Isaacs	United States
Jidong	Jia	China
François	Jornayvaz	Switzerland
Fasiha	Kanwal	United States
Cynthia	Kemp	United States
Denise	Kile	United States
Won	Kim	South Korea
Seung Up	Kim	South Korea
George	KK Lau	Hong Kong
Samuel	Klein	United States
David	Kleiner	United States
Rohit	Kohli	United States
Bart	Koot	Netherlands
Yannoula	Koulla	Cyprus
Marcelo	Kugelmas	United States
Joel	Lavine	United States
Jeffrey	Lazarus	Spain
Mariana	Lazo	United States
Hye Won	Lee	South Korea
Nathalie	Leite	Rio de Janeiro
Han-Chieh	Lin	Taiwan
Michelle	Long	United States
Rohit	Loomba	United States
Susan	Love Hawfield	United States
Adelina	Lozano	Peru
Panu	Luukkonen	Finland
Paula	Macedo	Portugal
Dina	Mansour	United Kingdom
Christos	Mantzoros	United States
Giulio	Marchesini	Italy
Sebastián	Marciano	Buenos Aires

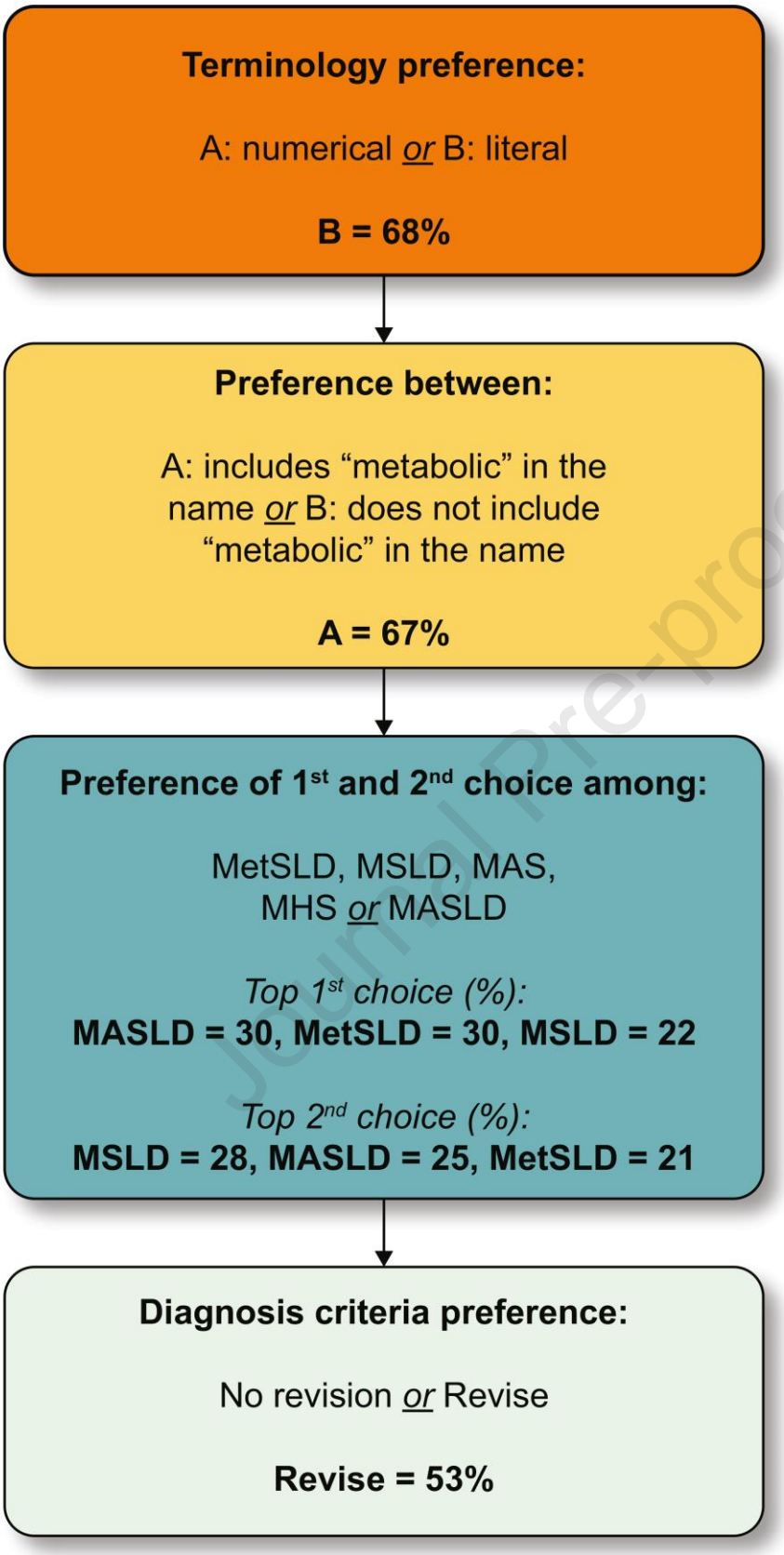
Claudia P.	Marques Souza de Oliveira	Brazil
Kim	Martinez	United States
Lyudmila Vladimirova	Mateva	Bulgaria
Jose M	Mato	Spain
Alexis	McCary	United States
Jeff	McIntyre	United States
Luca	Miele	Italy
Ivana	Mikolasevic	Croatia
Veronica	Miller	United States
Pam	Miller	United States
Maria "Terri"	Milton	United States
Milan	Mishkovikj	North Macedonia
Robert	Mitchell-Thain	United Kingdom
Rosalba	Moreno	United States
Timothy	Morgan	United States
Cynthia	Moylan	United States
Atsushi	Nakajima	Japan
Jean Charles	Nault	France
Phil	Newsome	United Kingdom
Suzanne	Norris	Ireland
Mazen	Noureddin	United States
Claudia P.	Oliveira	Brazil
Massao	Omata	Japan
Arlin	Ong	Philippines
Martín	Padilla	Perú
Raluca	Pais	France
Arturo	Panduro	Mexico
Manas K	Panigrahi	India
George	Papatheodoridis	Greece
Edison	Parise	Brazil
Sonali	Paul	United States
Diana	Payawal	Philippines
Serena	Pelusi	Italy
Marlene	Pérez	Brazil
Juanita	Perez Escobar	Mexico
Gianluca	Perseghin	Italy
Mario	Pessoa	Brazil
Salvatore	Petta	Italy
Massimo	Pinzani	United Kingdom
Monica	Platon Lupsor	Romania
Atoosa	Rabiee	United States
Vlad	Ratziu	France
Mario R.	Alvares-da-Silva	Brazil
Mary	Rinella	United States
Michael	Roden	Germany

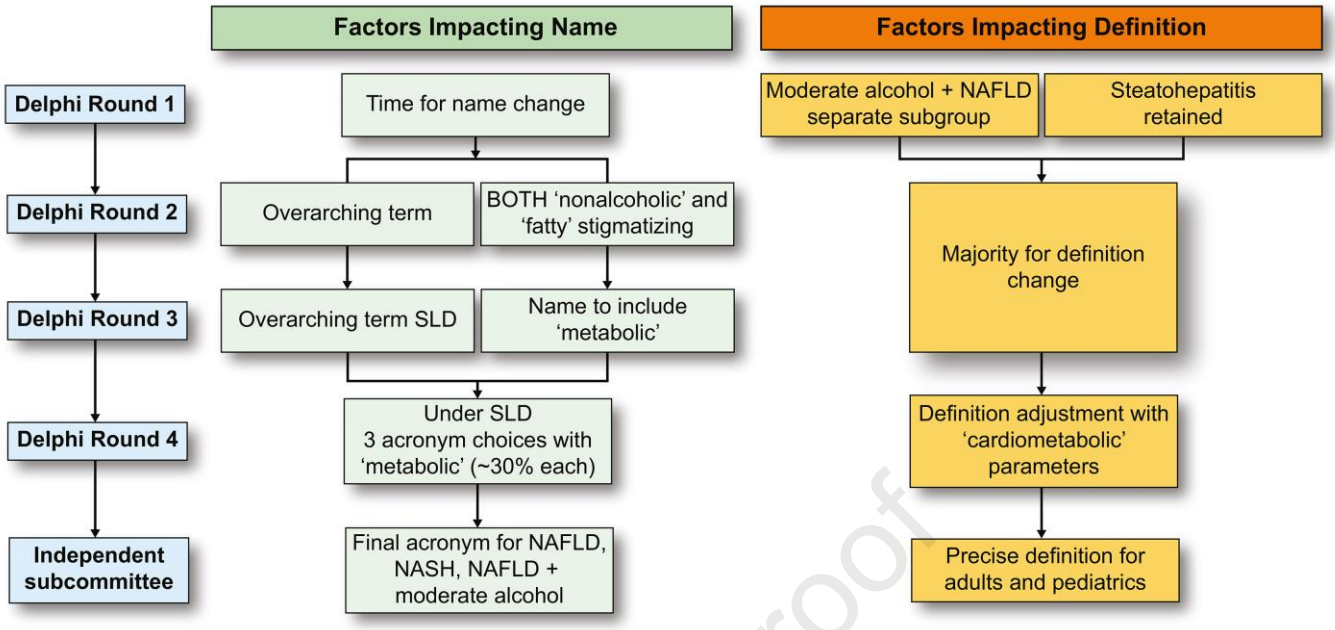
Stefano	Romeo	Sweden
Manuel	Romero Gomez	Spain
Yaron	Rotman	United States
Ian	Rowe	United Kingdom
Riina	Salupere	Estonia
Arun	Sanyal	United States
Shiv Kumar	Sarin	India
Sanjaya K.	Satapathy	United States
Jörn M.	Schattenberg	Germany
Wendy	Schaufert	Canada
Bernd	Schnabl	United States
Jeff	Schwimmer	United States
Lynn	Seim	United States
Lawrence	Serfaty	France
David	Shapiro	United States
Marcelo	Silva	Buenos Aires
Ashwani K.	Singal	United States
Shivaramn Prasad	Singh	India
Lubomir	Skladany	Slovakia
Silvia	Sookoian	Argentina
Norbert	Stefan	Germany
Jonathan	Stine	United States
Shikha	Sundaram	United States
C. Wendy	Spearman	South Africa
Gianluca	Svegliati-Baroni	Italy
Gyonzgi	Szabo	United States
Frank	Tacke	Germany
Tawesak	Tanwandee	Thailand
Giovanni	Targher	Italy
Brent	Tetri	United States
Maja	Thiele	Denmark
Dina	Tiniakos	Greece
Baron	Tisthammer	United States
Aldo	Torre Delgadillo	Mexico
Diane	Tovar	United States
Michael	Trauner	Austria
Emmanuel	Tsochatzis	United Kingdom
Luca	Valenti	Italy
Laurens	Van Kleef	Netherlands
Saskia	Van Mil	Netherlands
Lisa	VanWagner	United States
Adriana	Varon Puerta	Colombia
Jose Antonio	Velarde Ruiz Velasco	Mexico
Mette	Vesterhus	Norway
Eduardo	Vilar-Gomez	United States
Anthony	Villiotti	United States

Miriam	Vos	United States
Kymberly	Watt	United States
Julia	Wattacheril	United States
Fonda	Wilkins	United States
José	Willemse	Netherlands
Vincent	Wong	China
Stavra	Xanthakos	United States
Yusuf	Yilmaz	Turkey
Lorna	Younger	United States
Zobair	Younossi	United States
Amany	Zekry	United Kingdom
Shira	Zelber-Sagi	Israel



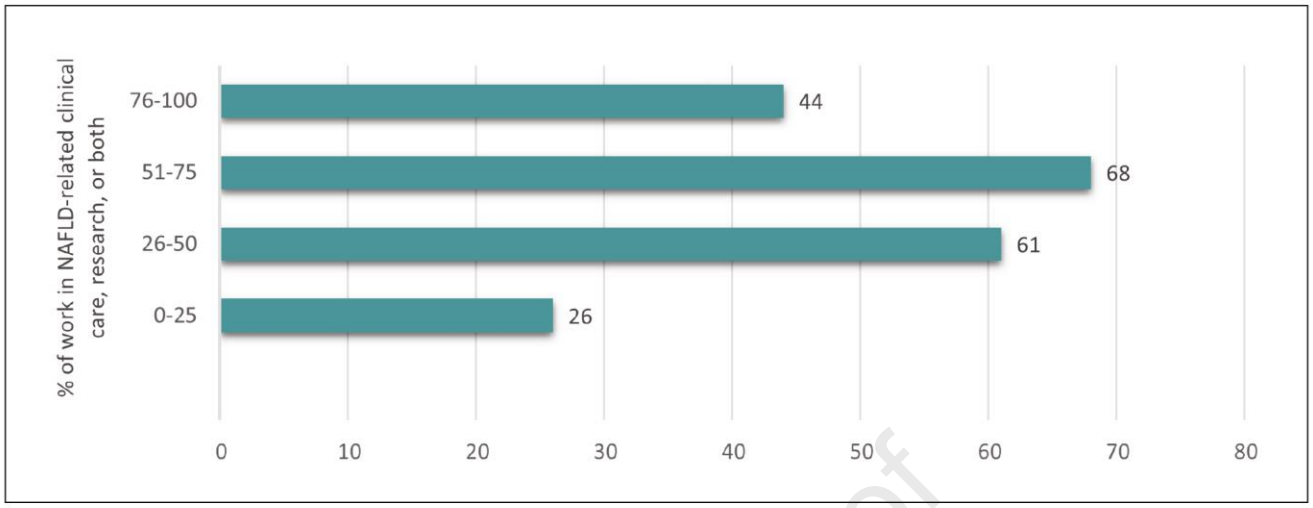
*Weekly intake 140-350g female, 210-420g male (average daily 20-50g female, 30-60g male)
**e.g. Lysosomal Acid Lipase Deficiency (LALD), Wilson disease, hypobetalipoproteinemia, inborn errors of metabolism
***e.g. Hepatitis C virus (HCV), malnutrition, celiac disease



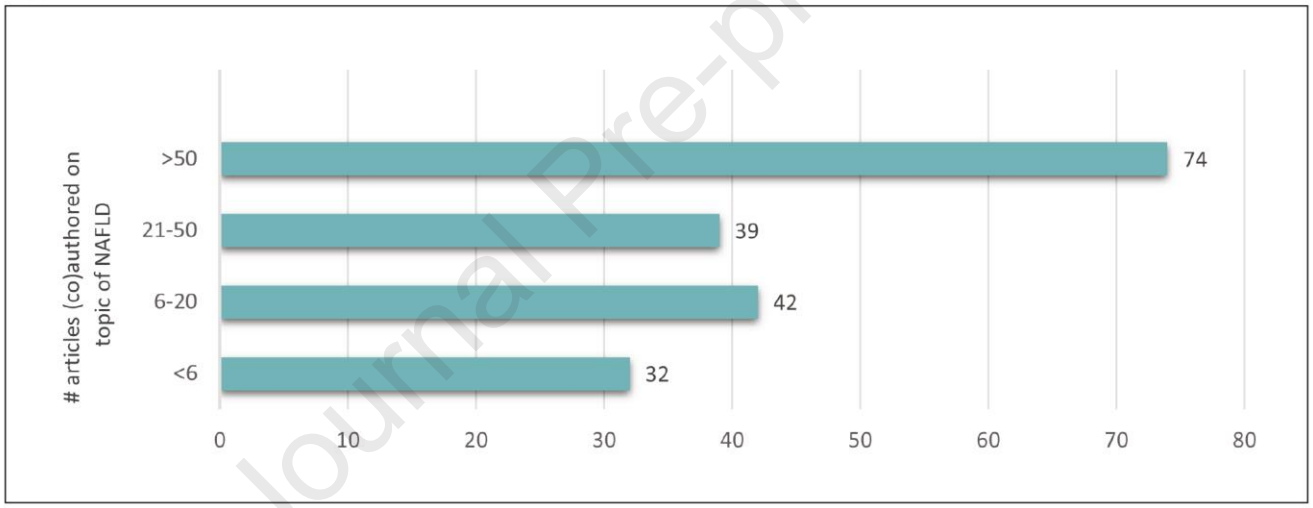


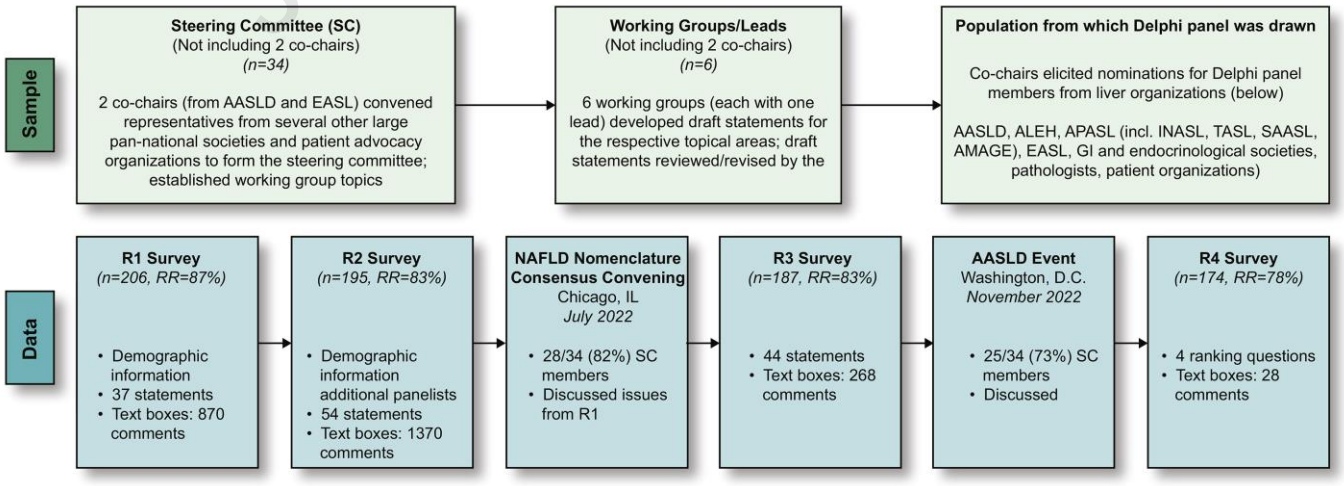
Legend: the flow chart on the left illustrates the evolution in decision-making as regards naming, whereas the one on the right illustrates decision-making as regards definition.

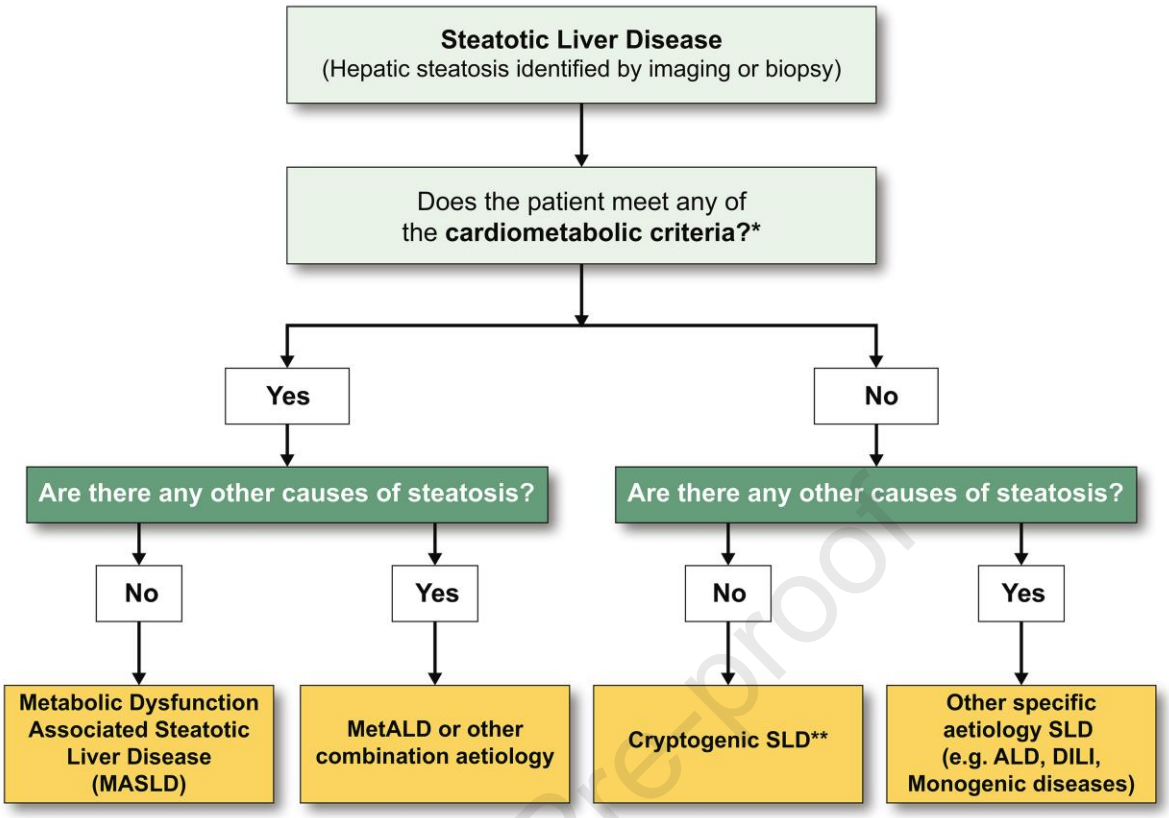
A



B







***Cardiometabolic criteria**

Adult Criteria	Pediatric Criteria
At least 1 out of 5:	**At least 1 out of 5:**
☐ BMI ≥ 25 kg/m² [23 Asia] **OR** WC > 94 cm (M) 80 cm (F) **OR** ethnicity adjusted	☐ BMI ≥ 85th percentile for age/sex [BMI z score ≥ +1] **OR** WC > 95th percentile **OR** ethnicity adjusted
☐ Fasting serum glucose ≥ 5.6 mmol/L [100 mg/dL] **OR** 2-hour post-load glucose levels ≥ 7.8 mmol/L [≥140 mg/dL] **OR** HbA1c ≥ 5.7% [39 mmol/L] **OR** type 2 diabetes **OR** treatment for type 2 diabetes	☐ Fasting serum glucose ≥ 5.6 mmol/L [≥ 100 mg/dL] **OR** serum glucose ≥ 11.1 mmol/L [≥ 200 mg/dL] **OR** 2-hour post-load glucose levels ≥ 7.8 mmol [140 mg/dL] **OR** HbA1c ≥ 5.7% [39 mmol/L] **OR** already diagnosed/treated type 2 diabetes **OR** treatment for type 2 diabetes
☐ Blood pressure ≥ 130/85 mmHg **OR** specific antihypertensive drug treatment	☐ Blood pressure age < 13y, BP ≥ 95th percentile **OR** ≥ 130/80 mmHg (whichever is lower); age ≥ 13y, 130/85 mmHg **OR** specific antihypertensive drug treatment
☐ Plasma triglycerides ≥ 1.70 mmol/L [150 mg/dL] **OR** lipid lowering treatment	☐ Plasma triglycerides < 10y, ≥ 1.15 mmol/L [≥ 100 mg/dL]; age ≥ 10y, ≥ 1.70 mmol/L [≥ 150 mg/dL] **OR** lipid lowering treatment
☐ Plasma HDL-cholesterol ≤ 1.0 mmol/L [40 mg/dL] (M) and ≤ 1.3 mmol/L [50 mg/dL] (F) **OR** lipid lowering treatment	☐ Plasma HDL-cholesterol ≤ 1.0 mmol/L [≤ 40 mg/dL] **OR** lipid lowering treatment