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SPECIAL ARTICLE

OPEN

A global action agenda for turning the tide on fatty liver disease

Jeffrey V. Lazarus^{1,2,3}  | Henry E. Mark^{4,5}  | Alina M. Allen⁶  |
 Juan Pablo Arab^{7,8,9}  | Patrizia Carrieri¹⁰  | Mazen Nouredin¹¹  |
 William Alazawi¹²  | Naim Alkhouri¹³  | Saleh A. Alqahtani¹⁴  |
 Quentin M. Anstee¹⁵  | Marco Arrese⁹ | Ramon Bataller¹⁶  |
 Thomas Berg¹⁷  | Paul N. Brennan¹⁸  | Patrizia Burra¹⁹  |
 Graciela E. Castro-Narro^{20,21,22}  | Helena Cortez-Pinto²³  | Kenneth Cusi²⁴  |
 Nikos Dedes²⁵ | Ajay Duseja²⁶  | Sven M. Francque^{27,28}  |
 Amalia Gastaldelli²⁹  | Hannes Hagström³⁰  | Terry T.K. Huang^{3,31}  |
 Dana Ivancovsky Wajcman¹  | Achim Kautz³² | Christopher J. Kopka³³  |
 Aleksander Krag³⁴  | Philip N. Newsome³⁵  | Mary E. Rinella³⁶ |
 Diana Romero³⁷  | Shiv Kumar Sarin³⁸  | Marcelo Silva³⁹ |
 C. Wendy Spearman⁴⁰  | Norah A. Terrault⁴¹  | Emmanuel A. Tsochatzis⁴²  |
 Luca Valenti^{43,44}  | Marcela Villota-Rivas¹  | Shira Zelber-Sagi^{45,46} |
 Jörn M. Schattenberg⁴⁷  | Vincent Wai-Sun Wong⁴⁸  | Zobair M. Younossi⁴⁹  |
 on behalf of the *Healthy Livers, Healthy Lives Collaborators*

¹Barcelona Institute for Global Health (ISGlobal), Hospital Clínic, University of Barcelona, Barcelona, Spain²Faculty of Medicine and Health Sciences, University of Barcelona, Barcelona, Spain³CUNY Graduate School of Public Health and Health Policy (CUNY SPH), New York, New York, USA⁴European Association for the Study of the Liver (EASL), Geneva, Switzerland⁵Independent consultant, Nottingham, UK⁶Department of Medicine, Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, Minnesota, USA⁷Department of Medicine, Division of Gastroenterology, Schulich School of Medicine, Western University & London Health Sciences Centre, London, Ontario, Canada⁸Department of Epidemiology and Biostatistics, Schulich School of Medicine, Western University, London, Ontario, Canada⁹Department of Gastroenterology, School of Medicine, Pontificia Universidad Católica de Chile, Santiago, Chile¹⁰Aix Marseille Univ, Inserm, IRD, SESSTIM, Sciences Economiques & Sociales de la Santé & Traitement de l'Information Médicale, ISSPAM, Marseille, France¹¹Houston Methodist Hospital, Houston Research Institute, Houston, Texas, USA¹²Barts Liver Centre, Blizard Institute, Queen Mary University of London, London, UK¹³Fatty Liver Program, Arizona Liver Health, Phoenix, Arizona, USA¹⁴King Faisal Specialist Hospital & Research Centre, Riyadh, Saudi Arabia¹⁵Translational & Clinical Research Institute, Faculty of Medical Sciences, Newcastle University, Newcastle upon Tyne, UK¹⁶Liver Unit, Hospital Clínic, University of Barcelona, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain¹⁷Department of Medicine II, Division of Hepatology, Leipzig University Medical Center, Leipzig, Germany¹⁸Division of Hepatology, University of Dundee, Dundee, Scotland, UK¹⁹Multivisceral Transplant Unit-Gastroenterology, Department of Surgery, Oncology and Gastroenterology at the Padua University Hospital, Padua, Italy²⁰Department of Hepatology and Transplant, Hospital Médica Sur, Mexico City, Mexico

- ²¹Department of Gastroenterology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico
- ²²Asociación Latinoamericana para el Estudio del Hígado (ALEH), Santiago, Chile
- ²³Clinica Universitária de Gastreterologia, Laboratório de Nutrição, Faculdade de Medicina, Universidade de Lisboa, Lisbon, Portugal
- ²⁴Department of Medicine, Division of Endocrinology, Diabetes & Metabolism, University of Florida, Gainesville, Florida, USA
- ²⁵Greek Patients Association, Athens, Greece
- ²⁶Department of Hepatology, Postgraduate Institute of Medical Education and Research, Chandigarh, India
- ²⁷Department of Gastroenterology and Hepatology, Antwerp University Hospital, Edegem, Belgium
- ²⁸InflaMed 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
- ²⁹Institute of Clinical Physiology, National Research Council, Pisa, Italy
- ³⁰Department of Medicine, Huddinge, Karolinska Institutet, Stockholm, Sweden
- ³¹CUNY Center for Systems and Community Design and NYU-CUNY Prevention Research Center, New York, New York, USA
- ³²Kautz 5 gUG, Köln, Germany
- ³³Independent researcher, Ponte de Lima, Portugal
- ³⁴Department of Gastroenterology and Hepatology, Odense University Hospital, Odense, Denmark
- ³⁵National Institute for Health Research Birmingham Biomedical Research Centre at University Hospitals Birmingham NHS Foundation Trust and the University of Birmingham, Birmingham, UK
- ³⁶Department of Medicine, University of Chicago, Chicago, Illinois, USA
- ³⁷Department of Community Health and Social Sciences, CUNY Graduate School of Public Health and Health Policy, New York, New York, USA
- ³⁸Department of Hepatology, Institute of Liver and Biliary Sciences, New Delhi, India
- ³⁹Hepatology and Clinical Research Units, Hospital Universitario Austral, Buenos Aires, Argentina
- ⁴⁰Department of Medicine, Division of Hepatology, Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa
- ⁴¹Gastrointestinal and Liver Disease Division, University of Southern California, Los Angeles, California, USA
- ⁴²UCL Institute for Liver and Digestive Health, Royal Free Hospital, London, UK
- ⁴³Precision Medicine, Biological Resource Center, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
- ⁴⁴Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy
- ⁴⁵School of Public Health, Faculty of Social Welfare and Health Sciences, University of Haifa, Haifa, Israel
- ⁴⁶Department of Gastroenterology, Tel Aviv Medical Centre, Tel Aviv, Israel
- ⁴⁷Metabolic Liver Research Program, I. Department of Medicine, University Medical Centre Mainz, Mainz, Germany
- ⁴⁸The Chinese University of Hong Kong, Hong Kong, China
- ⁴⁹Center for Liver Disease, Inova, Falls Church, Virginia, USA

Correspondence

Jeffrey V. Lazarus, CUNY Graduate School of Public Health and Health Policy (CUNY SPH), New York, NY, USA.

Email: Jeffrey.Lazarus@sph.cuny.edu

Abstract

Background and Aims: Fatty liver disease is a major public health threat due to its very high prevalence and related morbidity and mortality. Focused and dedicated interventions are urgently needed to target disease prevention, treatment, and care.

Approach and Results: We developed an aligned, prioritized action agenda

Abbreviations: AASLD, American Association for the Study of Liver Diseases; A, agree; ALEH, Asociación Latinoamericana para el Estudio del Hígado (Latin American Association for the Study of the Liver); APASL, Asian Pacific Association for the Study of the Liver; D, disagree; EASL, European Association for the Study of the Liver; N, total number of responses; NQ, the percentage of participants that indicated that they were not qualified to respond; SA, somewhat agree; SD, somewhat disagree.

Jeffrey V. Lazarus, Henry E. Mark, Alina M. Allen, Juan Pablo Arab, Patrizia Carrieri, and Mazen Nouredin contributed equally as first authors.

Jörn M. Schattenberg, Vincent Wai-Sun Wong, and Zobair M. Younossi contributed equally as senior authors.

The full list of *Healthy Livers*, *Healthy Lives* Collaborators (ie, the full authorship list) starts on page 17.

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for the global fatty liver disease community of practice. Following a Delphi methodology over 2 rounds, a large panel (R1 n = 344, R2 n = 288) reviewed the action priorities using Qualtrics XM, indicating agreement using a 4-point Likert-scale and providing written feedback. Priorities were revised between rounds, and in R2, panelists also ranked the priorities within 6 domains: epidemiology, treatment and care, models of care, education and awareness, patient and community perspectives, and leadership and public health policy. The consensus fatty liver disease action agenda encompasses 29 priorities. In R2, the mean percentage of “agree” responses was 82.4%, with all individual priorities having at least a super-majority of agreement (> 66.7% “agree”). The highest-ranked action priorities included collaboration between liver specialists and primary care doctors on early diagnosis, action to address the needs of people living with multiple morbidities, and the incorporation of fatty liver disease into relevant non-communicable disease strategies and guidance.

Conclusions: This consensus-driven multidisciplinary fatty liver disease action agenda developed by care providers, clinical researchers, and public health and policy experts provides a path to reduce the prevalence of fatty liver disease and improve health outcomes. To implement this agenda, concerted efforts will be needed at the global, regional, and national levels.

INTRODUCTION

NAFLD, hereafter referred to simply as fatty liver disease, is the most widespread liver disease, with an estimated prevalence of 38% of the global adult population^[1] and around 13% of children and adolescents.^[2] The disease is an increasingly important contributor to global morbidity and mortality, emphasized by the substantial increase in fatty liver disease-related cirrhosis over the past decade.^[3] The disease, which shares common metabolic risk factors with obesity, diabetes, and cardiovascular disease,^[4,5] causes far-ranging health, social, and economic consequences that impact at the individual, community, and population levels.^[6–8]

Despite excess fat in the liver (hepatic steatosis) in the early stages of the disease, affected individuals generally experience few, nonspecific, symptoms (eg, fatigue, abdominal pain), commonly leading to a delayed diagnosis and worse health outcomes.^[9] More broadly, the asymptomatic nature of the disease manifests through a generalized lack of urgency and policies to tackle the issue.^[10]

The burden of fatty liver disease is expected to grow in the coming decades^[11] with wide-ranging implications for public health and health systems, yet countries are ill-prepared to face this challenge. A 2020 survey of 102 countries found that no country had a written strategy to address fatty liver disease, and around one-third of

countries scored zero on a policy preparedness index.^[12] In the same year, a consortium of 218 experts from 91 countries published a set of recommendations to advance the public health and policy agenda, including a call for a global coalition to lead the development of a public health roadmap for fatty liver disease.^[13]

Fatty liver disease represents a contemporary public health challenge that requires multidisciplinary and multi-sectoral responses and novel collaboration, from re-orienting health systems to addressing food systems, the built environment, and social deprivation.^[14] For policymakers, practitioners, industry, and patient advocates, this represents unique challenges as they seek to embrace the complexity and scale of the problem with the need for effective and efficient responses.^[15] Building on earlier work, this study engaged a global multidisciplinary group of experts to develop a set of consensus actions, which can collectively turn the tide on this silent but challenging public health threat.

METHODS

This study employed a Delphi methodology to develop consensus action priorities for fatty liver disease. The same global consortium previously published 28 research priorities following the same methodology.^[16]

The 9 co-chairs identified 33 experts, covering clinical care and research, public health and policy, and advocacy, who collectively formed the core author group ($n = 42$) (Supplementary Table 1, <http://links.lww.com/HEP/H907>). The core group identified experts who formed the survey panel ($n = 473$) (Figure 1; Table 1). All participants had expertise in the field of fatty liver disease, non-communicable diseases (NCDs), and/or consensus methodologies. The core group drew on participants from earlier work, including the global NAFLD nomenclature process ($n = 240$),^[17] through which the American Association for the Study of Liver Diseases, the Latin American Association for the Study of the Liver (Asociación Latinoamericana para el Estudio del Hígado), the Asian Pacific Association for the Study of the Liver, and the European Association for the Study of the Liver nominated participants. Panelists were also identified from past NAFLD consensus efforts^[13] and the Wilton Park and Economist Intelligence Unit projects through the EASL International Liver Foundation.

Drafting of action priorities

Part of the core group ($n = 20$) reviewed the literature and evidence base, then developed a set of evidence briefs around 7 topics, summarizing the current knowledge base, envisioning what “success” would look like in the next decade, identifying key questions, and suggesting action priorities for (1) the human and economic burden; (2) defining and implementing models of care; (3) treatment and care; (4) education and awareness; (5) patient and community perspectives; (6) policy strategies and a societal approach; and (7) leadership for the fatty liver disease public health agenda. The briefs were debated during a 3-day roundtable at Wilton Park, UK, in October 2022—co-chaired by Henry E. Mark and opened by Thomas Berg and Jeffrey V. Lazarus—in which 26 core group members and 11 co-authors participated. The action priorities were subsequently revised by Jeffrey V. Lazarus and Henry E. Mark to reflect the Wilton Park discussions, and topics 6 and 7 were combined. The priorities were revised by core group members to reflect the discussions ahead of the first Delphi survey round (December 21, 2022 to January 15, 2023).

Delphi method data collection and analysis

The study design consisted of the Wilton Park meeting (Supplementary Table 2, <http://links.lww.com/HEP/H907>) and 2 survey rounds (R1 and R2). In both rounds, respondents indicated their agreement with each priority using a 4-point Likert-type scale (ie, “agree,” “somewhat agree,” “somewhat disagree,” and

“disagree”). Given the multidisciplinary nature of the panel, the survey included a fifth “not qualified to respond” option. Panelists could provide comments and suggest edits to individual priorities and provide overall comments at the end of each survey. Demographic data were collected in R1. The survey was distributed using the Qualtrics XM platform (round duration ranged from 2 to 3.5 wks).

An analytic team of core group members (Jeffrey V. Lazarus, Henry E. Mark, Paul N. Brennan, Christopher J. Kopka, Diana Romero, Dana Ivancovsky Wajcman, and Marcela Villota-Rivas) reviewed the R1 data, including 545 open-ended comments, and initiated revisions; the core group subsequently reviewed the revised priorities ahead of R2. In R2 (8–21 February 2023), panelists voted on the revised priorities and ranked at least half of the priorities within each of the 6 domains: epidemiology, models of care, treatment and care, education and awareness, patient and community perspectives, and leadership and public health policy.

Each action priority was graded to indicate the level of combined agreement (“agree” + “somewhat agree”), using a system that has been used in other Delphi studies^[13] in which “U” denotes unanimous (100%) agreement, “A” denotes 90%–99% combined agreement, “B” denotes 78%–89% combined agreement, and “C” denotes 67%–77% combined agreement. For the ranking, scores were calculated and normalized in Microsoft Excel (v.16.70) to compare rankings within each domain.

Ethical considerations

This study received an ethical review exemption from the Hospital Clínic of Barcelona, Spain, ethics committee on December 19, 2022. All research was conducted in accordance with both the Declarations of Helsinki and Istanbul. Panelists consented to participate in the study, and data were anonymized for all analyses.

RESULTS

A total of 473 individuals were invited to participate in R1, and 344 (72.7%) completed the survey. These 344 respondents were invited to participate in R2, of whom 288 (83.7%) completed the survey. Table 1 details the demographics of all expert panelists involved in the study. The mean age of respondents was 53.8 (SD: 10.1). Most respondents were male (64.8%), worked in high-income countries (69.9%) and in the Europe and Central Asia region (42.2%), were primarily employed in the academic sector (66.6%), and worked in the clinical research field (79.4%). A total of 94 countries were represented in terms of respondent country of origin and 91 in terms of respondent country of work.

TABLE 1 Delphi panel characteristics (n = 344).

Characteristic	n (%)
Sex	
Woman	115 (33.7)
Man	221 (64.8)
Non-binary or gender diverse	3 (0.9)
Prefer not to say	2 (0.6)
No response	3 (0.9)
Age, mean [SD]	
All	53.8 [10.1]
No response	12 (3.5)
Country of origin, by income level (n = 94)	
Low or middle	124 (36.9)
High	212 (63.1)
No response	8 (2.3)
Global region^a of origin	
East Asia and Pacific	37 (11.0)
Europe and Central Asia ^b	142 (42.3)
Latin America and Caribbean	41 (12.2)
Middle East and North Africa	28 (8.3)
North America	52 (15.5)
South Asia	19 (5.7)
Sub-Saharan Africa	17 (5.1)
No response	8 (2.3)
Country of work, by income level (n = 91)	
Low or middle	102 (30.1)
High	237 (69.9)
No response	5 (1.5)
Global region^a of work	
East Asia and Pacific	36 (10.6)
Europe and Central Asia ^c	143 (42.2)
Latin America and Caribbean	34 (10.0)
Middle East and North Africa	24 (7.1)
North America	76 (22.4)
South Asia	12 (3.5)
Sub-Saharan Africa	14 (4.1)
No response	5 (1.5)
Primary sector of employment^d	
Academic	229 (66.6)
Public	62 (18.0)
Private	38 (11.0)
Civil society	9 (2.6)
Other	3 (0.9)
No response	3 (0.9)
Field(s) of employment^{de}	
Clinical research	273 (79.4)
Non-clinical research	81 (23.5)
Healthcare provider	180 (52.3)
Patient/policy advocacy	36 (10.5)
Education	10 (2.9)
Other	7 (2.0)
No response	3 (0.9)

TABLE 1 (continued)

Characteristic	n (%)
Years working in fatty liver disease field	
1–11	148 (43.7)
12–22	132 (38.9)
23–33	49 (14.5)
34–44	8 (2.4)
45–55	2 (0.6)
No response	5 (1.5)
Publications authored focused on fatty liver disease	
< 6	103 (30.9)
6 to 25	95 (28.5)
26 to 50	54 (16.2)
51 to 100	42 (12.6)
> 100	39 (11.7)
No response	11 (3.2)
International or regional liver association membership(s)^e	
AASLD	165 (48.0)
APASL	34 (9.9)
ALEH	30 (8.7)
EASL	191 (55.5)
Other	18 (5.2)
No membership	152 (44.2)
Area of national professional association/society membership(s) in the country of work^e	
Liver disease	254 (73.8)
Gastroenterology	184 (53.5)
Obesity	42 (12.2)
Diabetes/Endocrinology	45 (13.1)
Heart disease	11 (3.2)
Cancer	15 (4.4)
Primary care	5 (1.5)
Other	26 (7.6)
No membership	25 (7.3)

Notes: Percentages for 'no response' are based on the total number of participants; all other percentages are calculated after excluding n of no response, unless otherwise indicated.

Percentages may sum to more than 100 due to rounding.

^aBased on World Bank regions.

^bn = 3 participants are originally from Central Asia.

^cn = 3 participants work in Central Asia.

^dDenominator includes n of no response.

^eSum may exceed the sample size as participants could choose > 1 response.

Abbreviations: AASLD, American Association for the Study of Liver Diseases; ALEH, Asociación Latinoamericana para el Estudio del Hígado (Latin American Association for the Study of the Liver); APASL, Asian Pacific Association for the Study of the Liver; EASL, European Association for the Study of the Liver.

In R1, 27 initial action priorities were presented to the panel. During revisions ahead of R2, 2 additional action priorities were included, with the panel reviewing 29 priorities in R2. Across the 2 Delphi rounds, combined agreement ("agree" + "somewhat agree") increased for all domains. The mean percentage of "agree" responses across domains increased from 80.0% in

R1 to 82.4% in R2, following the consideration of substantive comments received in R1.

Table 2 presents the final priorities, agreement grades, and rankings for each of the 6 domains. Within the final priorities in R2 (Figure 2), the panel reached a unanimous combined agreement for 2 priorities and > 90% combined agreement for the remaining 27; the mean level of combined agreement across all priorities was 98.1% (rising from 96.8% in R1). For 11 priorities, “agree” answers were < 80%, with higher reliance on “somewhat agree” to achieve the high rate of overall combined agreement (Supplementary Table 3, <http://links.lww.com/HEP/H907>). Defining and implementing models of care and treatment and care were the 2 domains where more than half of the action priority statements had < 80% of the panel “agree”; all of these statements received > 90% combined agreement but relied more heavily on the “somewhat agree” category to achieve this. All of the action priorities received at least a super-majority (66.7%) of “agree” in R2.

DISCUSSION

Fatty liver disease has far-reaching health, social, and economic consequences,^[3,6,7,18] which, without urgent efforts, will continue to grow.^[11] Heeding earlier calls for further collaboration,^[10,13] this study employed an inclusive and responsive methodology to develop a multidisciplinary action agenda for stakeholders around the world. As noted previously, this work follows different yet complementary work on setting a global research agenda for fatty liver disease.^[16] Below, we discuss the 29 agreed-upon actions within 6 overarching domains.

Domain 1: The human and economic burden

Both the clinical and economic burden of fatty liver disease continue to increase. The prevalence of the disease has grown dramatically in recent decades, becoming an increasingly important contributor to morbidity and mortality.^[3] The economic burden is vast; data from several high-income countries show the scale of direct health care costs in both out-patient^[19] and in-patient settings^[20] and the wider societal costs.^[6,7,21] While data from a broader range of contexts, including resource-limited settings, will strengthen our understanding, what we know today about the human and economic consequences of this disease present a compelling case for action.

A prior consensus statement from the liver health community noted the increased costs associated with fatty liver disease while also accepting that “incomplete data hinder concerted action at the national and global levels”.^[13] In this study, panelists proposed 2 priorities intending to deepen understanding and action with respect to the human and economic burden. The highest-ranked priority within this domain reflects the need to promote standardization and harmonization of data collection and reporting on the human and economic burden (priority 1.2) to allow for meaningful comparisons. The panelists also agreed with prioritizing the development of investment cases for fatty liver disease (priority 1.1). Such investment cases will provide an empirical investigation of the human and economic burden associated with fatty liver disease, alongside estimations of expenses associated with reducing the human and economic burden. These can be key tools for engaging policymakers around not only

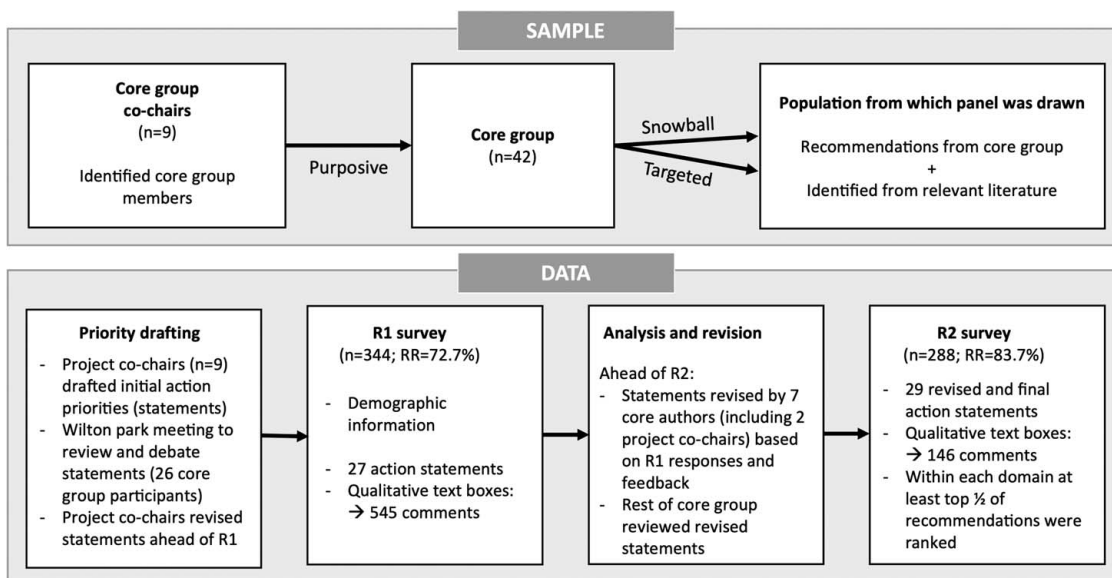


FIGURE 1 Delphi panel generation and data collection.

TABLE 2 Consensus statements for a fatty liver disease action priorities agenda.

Statement	Grade	Rank	A (%)	SA (%)	A + SA (%)	SD (%)	D (%)	NQ (%)	N	
Domain 1: The human and economic burden										
1.1	Develop national and international investment cases to inform evidence-based action and advocacy on fatty liver disease.	A	2	69.3	27.9	97.2	2.4	0.3	0.3	287
1.2	Promote standardization of data collection and reporting on the human and economic burden of fatty liver disease to enable comparisons across different groups, populations, and settings.	A	1	87.8	11.2	99.0	0.3	0.7	0.7	286
Domain 2: Defining and implementing models of care										
2.1	Engage affected populations and people with lived experience in the design of patient-centered fatty liver disease models of care.	A	—	71.1	24.7	95.8	3.5	0.7	0.3	287
2.2	Implement community-tailored models of care for fatty liver disease diagnosis, prevention, and treatment.	A	3	78.0	20.9	99.0	1.0	0.0	0.3	287
2.3	Inform health system decision-makers of the operational and financial implications of emerging and evolving fatty liver disease models of care.	U	—	78.4	21.3	99.7	0.0	0.3	0.3	287
2.4	Develop a range of context-specific and resource-specific fatty liver disease multidisciplinary model of care examples to promote evidence-based knowledge sharing of good practices.	A	4	76.6	21.0	97.6	1.7	0.7	0.7	286
2.5	Clinical societies/health authorities should develop clear guidance on care pathways that promote the timely referral of fatty liver disease patients within health care settings.	A	2	87.5	11.5	99.0	0.7	0.3	0.3	287
2.6	Liver specialists should collaborate with primary care experts to determine which noninvasive tests are most appropriate for use in primary care settings.	A	1	94.1	4.9	99.0	1.0	0.0	0.0	287
2.7	Standardize key metrics for assessing and evaluating fatty liver disease models of care.	A	—	83.3	16.0	99.3	0.3	0.3	0.0	288
Domain 3: Treatment and care										
3.1	Account for the social and commercial determinants of health when developing treatment and care strategies for people with fatty liver disease.	A	—	68.1	29.5	97.6	1.7	0.7	0.0	288
3.2	Develop tools to support the uptake of non-pharmacological interventions to improve outcomes in people with fatty liver disease.	A	1	87.5	11.5	99.0	1.0	0.0	0.0	288
3.3	Engage all relevant stakeholders (eg, providers, patients) for focused discussions with regulatory bodies on suggested endpoints for drug approval.	A	2	78.7	19.2	97.9	2.1	0.0	0.3	287
3.4	Increase the use of patient-reported outcomes in clinical and research settings and include these as primary study outcomes alongside clinical outcomes.	A	—	67.7	25.3	93.0	6.3	0.7	0.3	285
Domain 4: Education and awareness										
4.1	Evaluate medical curricula to identify how fatty liver disease is taught in medical schools and postgraduate training programs.	A	—	76.7	20.5	97.2	1.7	1.0	0.0	288
4.2	Expand the availability of educational courses and toolkits on fatty liver disease, including through formal medical curricula and continuing education, in collaboration with other disciplines.	U	4	85.4	14.2	99.7	0.0	0.3	0.0	288
4.3	Disseminate educational resources on the implementation of noninvasive tests in different settings, including primary care, diabetes, and obesity clinics, tailoring the content to the audience.	A	2	89.2	9.7	99.0	1.0	0.0	0.0	288

4.4	Develop information products to communicate how liver function and metabolic health influence overall population health.	A	—	81.6	17.7	99.3	0.3	0.3	0.0	288
4.5	Promote awareness among health care providers and patients of the possibility of multiple diagnoses (eg, fatty liver disease and type 2 diabetes mellitus and/or alcohol-associated liver disease) and accompanying challenges and opportunities in treatment and care.	A	1	92.0	6.6	98.6	0.7	0.7	0.0	288
4.6	Develop strategies with pediatric professionals to raise awareness of the challenges of fatty liver disease in children and adolescents.	A	—	88.5	10.1	98.6	1.1	0.4	3.1	278
4.7	Raise awareness of fatty liver disease through public campaigns, leveraging traditional media, social media, and collaborative approaches.	A	3	83.0	13.5	96.5	2.8	0.7	0.0	288
4.8	Inform all patients with fatty liver disease of their disease stage and educate them on the reversibility of liver fibrosis.	A	—	89.2	8.7	97.9	2.1	0.0	0.0	288
Domain 5: Patient and community perspectives										
5.1	Grow the networks of support for people with fatty liver disease, including through collaboration with existing patient groups (eg, liver, obesity, diabetes, heart disease, cancer).	A	1	83.3	14.6	97.9	1.7	0.3	0.3	287
5.2	Co-create, with affected communities and patient advocates, non-stigmatizing communication guides for health care professionals to use when engaging with fatty liver disease patients.	A	2	74.7	22.2	96.9	2.4	0.7	0.0	288
Domain 6: Leadership and policies for the fatty liver disease public health agenda										
6.1	Further develop collaborations with key stakeholders (eg, diabetes, obesity) to deliver an aligned non-communicable disease agenda, inclusive of fatty liver disease.	A	2	92.0	7.3	99.3	0.7	0.0	0.0	288
6.2	Advocate for fatty liver disease to be incorporated into relevant non-communicable disease strategies and guidelines, including those published by the World Health Organization.	A	1	92.0	6.9	99.0	0.7	0.3	0.0	288
6.3	Support professional societies' initiatives to identify emerging clinical and public health leaders in the field of fatty liver disease.	A	—	83.3	13.9	97.2	2.1	0.7	0.0	287
6.4	Convene groups of multidisciplinary experts to consider these research and action priorities for adoption at local, national, and regional levels.	A	—	86.8	12.2	99.0	1.0	0.0	0.0	288
6.5	Establish a global coalition, led by professional societies, to foster ongoing discussion, partnerships, and action, to address the fatty liver disease global public health threat.	A	3	85.4	12.5	97.9	1.0	1.0	0.0	288
6.6	The global coalition should build and execute a strategy to grow and expand the global community of practice (professional and voluntary) focused on reducing the burden of fatty liver disease.	A	—	79.8	18.5	98.3	0.3	1.4	0.3	287
Mean % agreement		—	—	82.4	15.7	98.1	—	—	—	—

Notes: Percentages may add up to more than 100 due to rounding. Grades are based on the percentage of combined agreement (agree + somewhat agree). U, unanimous (100%) agreement; A, 90%–99% agreement. Responses to each statement are presented as percentages of the total responses.

Abbreviations: A, agree; D, disagree; N, total number of responses; NQ, the percentage of participants that indicated that they were not qualified to respond; SA, somewhat agree; SD, somewhat disagree.



FIGURE 2 Action priorities to turn the tide on fatty liver disease.

the importance of action but the health and economic benefits of this.

Domain 2: Defining and implementing models of care

An important aspect of fatty liver disease is that the vast majority of patients can be cared for in primary care settings, whereas those with advanced fibrosis, or cirrhosis, need specialized care delivered by a multidisciplinary team.^[22] The availability of high-performing non-invasive tests (NITs) has now markedly reduced the need to rely on liver biopsy for the diagnostic and prognostic context of use,^[23,24] providing an effective and efficient way to identify patients at risk of poor hepatic-related outcomes.^[25]

Yet, it is acknowledged that most primary care settings are ill-equipped to effectively identify and refer patients at risk for advanced disease to secondary care as needed. Unsurprisingly, the highest-ranking priority within this domain focused on the need for liver specialists to collaborate with primary care experts to determine which NITs are most appropriate for use in primary care settings (priority 2.6), which is likely to differ between settings based on the resource availability and health system structure. Subsequently, providing clear guidance on care pathways and timely referrals was ranked second in this domain (priority 2.5). Along with the evolving refinement of NITs and referral

pathways, the panel agreed on the importance of standardization around key effectiveness measures to be used in the evaluation of multidisciplinary models of care (priority 2.7). These priorities sit alongside previous calls to generate data to validate NITs for early diagnosis, prognosis, and monitoring of liver disease progression.^[16]

Recognizing the shift within public policy and health systems toward person-centered care,^[26,27] engaging affected populations in the development of patient-centered care pathways (priority 2.1) and implementing community-tailored models of care for diagnosis, prevention, and treatment (priority 2.2, ranked 3rd in its domain) were determined to be priorities.

Emerging evidence suggests that a multidisciplinary approach to the management of fatty liver disease is imperative, although multidisciplinary care models are poorly adopted in most health care settings.^[22] Therefore, the panelists agreed that the development of a range of context-specific and resource-specific fatty liver disease multidisciplinary model of care examples (priority 2.4) was the fourth highest priority within the domain. As models of care for the disease emerge and evolve, panelists unanimously agreed on engaging with health system decision-makers about their operational and financial implications (priority 2.3). “Preventive hepatology”—first proposed in 2008—emphasizes the use of timely interventions to minimize adverse health outcomes of chronic liver disease.^[28] This is an important framing within fatty liver disease, given the

imperative of actively implementing a spectrum of strategies to prevent both disease onset and progression.

Taken together, the actions outlined in this domain will help to drive the much-needed knowledge and innovation in the management of this disease, which will inevitably place an increasing amount of pressure on health systems in the coming years.

Domain 3: Treatment and care

Notwithstanding current developments, including late-stage clinical trials for pharmacological treatments and bariatric procedures,^[29,30] the management of fatty liver disease remains highly dependent on weight reduction (targeting a sustained loss of at least 7%–10% of the initial body weight). However, barriers—such as insufficient knowledge and access to resources promoting a healthy lifestyle, physical discomfort, time constraints, and financial consideration—hinder the achievement of long-term weight loss goals. Thus, it is important to modify lifestyle risk factors (eg, nutrition, physical activity).^[31–33] These approaches target improvements in insulin resistance, optimizing glycemic control, and attenuating the pro-inflammatory milieu of obesity, which is a driver of disease progression.^[34]

To implement successful behavioral change, person-centered care and social interventions are needed. Motivational and self-monitoring approaches (eg, cognitive behavioral therapy, mindfulness-based stress reduction therapy) have shown positive outcomes in treating fatty liver disease.^[35] However, the social environment—which encompasses factors such as culture, gender, and socioeconomic status—also plays a significant role in obesity.^[36] The concept of social nutrition aims to promote a social environment that fosters improved metabolic health; this will be a critical concept to embed within actions for fatty liver disease care.

In anticipation of future pharmacological approvals, the panelists agreed on and ranked the development of tools to support pharmacological treatment uptake as the highest priority in this domain (priority 3.2). This work can draw inspiration from previous efforts in viral hepatitis.^[37] As the clinical trial space of NASH-specific drugs evolves, the appropriateness and utility of different trial end points, from the resolution of NASH or fibrosis regression to slowing disease progression, continues to be debated.^[38] The panel agreed that engaging relevant stakeholders, including patients, in focused discussions with regulators will help to advance the discourse around end points, ranking this as the second highest priority in this domain (priority 3.3). As similarly noted in other domains—and again consistent with patient-centric approaches—the panelists agreed with expanding the use of patient-reported outcomes

and including these alongside clinical outcomes within trials (priority 3.4). This is an emerging but rapidly expanding area within fatty liver disease.^[39]

The field of public health is also increasingly recognizing the role of commercial determinants of health^[40] alongside biological and social determinants.^[41] In light of this recognition, the panelists agreed that not only social but also commercial determinants of health should be prioritized when developing treatment and care strategies (priority 3.1). This work will require the liver health community to engage with those working across the NCD spectrum, including by lending their voice to existing calls for action to address negative commercial influences on public health.

Domain 4: Education and awareness

Available data on fatty liver disease awareness, while limited, illustrate low levels of public and patient awareness.^[38,42] Prior consensus statements from the liver health community have called for an increased strategic emphasis on education and awareness.^[13,16] In recognizing this evidence base and building on the prior consensus statements, the panelists agreed with 8 action priorities with respect to education and awareness for 4 broad audiences: (i) current health professionals, (ii) future health professionals, (iii) people living with fatty liver disease, and (iv) the general public.

The fatty liver disease continuum is bidirectional and inherently modifiable, sharing cardiometabolic features with several other NCDs (eg, obesity, diabetes, hypertension, cardiovascular disease).^[4,5] Yet, as noted, awareness among health care providers, at-risk patients, and policymakers is generally low. The highest-ranked action priority for this domain was cross-cutting, with panelists calling for promoting awareness among health care providers and patients of the possibility of multiple diagnoses (priority 4.5). The panel brought forward a second cross-cutting priority, calling for the development of informational products to communicate how liver function, and metabolic health, influence overall population health (priority 4.4).

Health care professionals and patients alike have reported a dearth of information about fatty liver disease and its management following diagnosis.^[43] Lack of awareness of the fibrosis stage is also emerging as being associated with lower adherence to lifestyle changes.^[44] With respect to affected populations, the panel agreed to inform all people with fatty liver disease of their disease stage and educate them on the reversibility of liver fibrosis (priority 4.8). With regards to the broader public, the panel supports awareness-raising through public campaigns, leveraging traditional media, social media, and collaborative approaches, ranking this as the third highest priority in the domain

(priority 4.7). This is particularly important considering the forthcoming change in NAFLD nomenclature.^[17]

As previously alluded to, NITs hold great promise for expanding the diagnosis of fatty liver disease. The panelists agreed to disseminate educational resources on the implementation of NITs in different settings (eg, primary care, diabetes, and obesity clinics) (priority 4.3, ranked 2nd in its domain). Recognizing that knowledge and awareness of fatty liver disease may be increased among some health professionals outside liver-specific environs, the panelists also unanimously agreed and ranked as the fourth highest priority to “expand the availability of educational courses and toolkits on fatty liver disease”; this could be achieved through “formal medical curricula and continuing education, in collaboration with other disciplines” (priority 4.2).

As the prevalence of fatty liver disease continues to expand not only among adults but also among children and adolescents,^[1,11] the panelists brought attention to and called for action on strategies for raising awareness in collaboration with pediatric professionals (priority 4.6).

Consistent with the strategic emphasis on expanding the fatty liver disease community of practice, further prioritized in a separate domain below, the panelists highlighted the need for education-oriented actions directed toward future health professionals through evaluating current medical curricula to identify how the disease is taught in both medical school and post-graduate training curricula (priority 4.1).

Domain 5: Patient and community perspectives

People living with fatty liver disease have unique support needs. A cohort study from 2023 demonstrated that low social support and loneliness (functional measures of social relationships) increased mortality risk in cirrhotic patients compared with noncirrhotic individuals.^[45] Addressing these barriers will be a major challenge, not least given the prevalence of the disease; however, with this comes the opportunity to innovate and transform fatty liver disease models of care. There is a wealth of experience that can be drawn on both within^[37] and outside of the liver health community to inform this work,^[46] including the World Health Organization frameworks on meaningful engagement of people living with NCDs^[27] and people-centered health care.^[47]

In step with this, the panelists agree to the importance of incorporating community perspectives, with 2 areas of early action emphasized. Firstly, the panel highlighted the importance of growing support networks for people with fatty liver disease (eg, patient groups) (priority 5.1) and, secondly, the need to co-create, with affected communities, non-stigmatizing communication guidance for health professionals to use when engaging people living with fatty liver disease (priority 5.2).

Domain 6: Leadership and policies for the fatty liver disease public health agenda

The consensus-built priorities for advancing the fatty liver disease public health agenda point to the importance of taking action that addresses the unique challenges posed by fatty liver disease and, crucially, that reflects the interlinked risks and solutions for fatty liver disease and other NCDs. Building on earlier calls for comprehensive public health and political efforts to counteract the growing fatty liver disease burden,^[13,16,48] this paper sets out a roadmap for action.

Public health and health systems increasingly face the complex challenges presented by growing multi-morbidity across NCDs,^[49] and fatty liver disease is no exception. Unsurprisingly, then, 2 of the 4 highest-scoring action priorities based on “agree” alone (priorities 6.1, ranked second in the domain and 6.2, ranked first in the domain) pertain to the inclusion of fatty liver disease in the strategies of other NCDs and advanced collaborations with stakeholders engaged with other NCDs (eg, diabetes, obesity).

There is growing clarity that more talent is needed to address the overall increasing burden of fatty liver disease.^[50] Unsurprisingly, the panelists called for a strategic approach to expand the fatty liver disease community of practice (priority 6.6), which will both broaden and deepen the expertise and talent within the community. As the community of practice expands, the panelists also advocated for nurturing the next generation of both clinical and public health leaders (priority 6.3) and convening multidisciplinary experts to enact these priorities at all levels (priority 6.4).

The panelists concurred that alongside national and regional efforts, there is a need for a coalition that can spearhead these efforts at the global level (priority 6.5, ranked third in its domain). Given the lack of awareness and attention provided to fatty liver disease within the broader global health discourse, the global coalition can foster discussion, partnerships, and action and provide a common platform for advancing this agenda. Early efforts to establish such a coalition have been instigated by regional liver associations (American Association for the Study of Liver Diseases, Asociación Latinoamericana para el Estudio del Hígado (Latin American Association for the Study of the Liver), the Asian Pacific Association for the Study of the Liver, and the European Association for the Study of the Liver) under the umbrella *Healthy Livers, Healthy Lives*.

Study strengths and limitations

As described within the research agenda developed by the same panel,^[16] the major strength of this study lies in its novelty as the first global, large-scale effort to propose a comprehensive action agenda for fatty liver disease.

Again, the group used the rigorous Delphi consensus process. This methodology allows degrees of agreement to be illustrated by breaking-out “agree/somewhat agree” and “somewhat disagree/disagree” responses, which the co-authors believe may assist decision-makers in government, industry, health systems, and across communities in their own prioritization efforts. We suggest that the scoping nature of the domains, combined with more refined actions, makes the outcome both globally relevant and operationally actionable.

While this study used the Delphi methodology, given its efficacy in consensus building, we note that multidisciplinary, action-oriented consensus are nonetheless challenging. This study used a purposive sampling of experts with prior experience in fatty liver disease, NCDs, and/or consensus methodologies in the development of the core group. To mitigate the biases of purposive sampling, the core group then used snowballing and targeted sampling to yield a geographically diverse, multidisciplinary panel of 344 people. However, we recognize that the panel's characteristics (eg, predominantly based in high-income countries and employed in the academic sector) will have influenced the study results. Notably, patient-centric and policy-oriented priorities had overall lower agreement levels, which likely reflects the smaller proportion of the panel whose primary field of work is patient and policy advocacy (n = 16, 4.7%). The chosen language for the study, English, may have also influenced those who accepted the invitation to contribute or the panelist's ability to fully comprehend every statement.

Conclusions

This study presents the first global consensus-built action agenda on fatty liver disease. Through a rigorous Delphi process, a large panel identified 29 unique action priorities across 6 domains. Taken together, these actions set out the collective efforts needed to arrest this growing but under-addressed public threat in the coming years. Critically, implementing these actions will require a fundamental shift in the liver field from a narrow focus on hepatology to a more comprehensive approach that includes various stakeholders from different medical specializations, such as endocrinology, primary care, and cardiology, alongside public health experts, social scientists, policymakers and governments, pharmaceutical and device industries, patient advocates, and, most importantly, patients themselves.

AUTHOR CONTRIBUTIONS

This study was led by a core group of 42 co-authors. Jeffrey V. Lazarus led the core group and provided regular updates by email. Twenty-six core group members and 11 co-authors participated in a 3-day

in-person meeting hosted by Wilton Park, UK, in October 2022, which informed the development of the action priorities included in the Delphi study. Seven of the co-chairs (Alina M. Allen, Juan Pablo Arab, Patrizia Carrieri, Mazen Nouredin, Jörn M. Schattenberg, Vincent Wai-Sun Wong, and Zobair M. Younossi) led the drafting of 7 evidence notes, including key priorities and challenges, ahead of the Wilton Park meeting and were supported by core group members (Ramon Bataller, Thomas Berg, Helena Cortez-Pinto, Kenneth Cusi, Nikos Dedes, Ajay Duseja, Terry T-K. Huang, Aleksander Krag, Philip N. Newsome, Mary E. Rinella, Marcelo Silva, Emmanuel A. Tsochatzis, and Shira Zelber-Sagi). The evidence notes were reviewed by Jeffrey V. Lazarus and Henry E. Mark and informed the drafting of the research and action priority statements. Diana Romero and Jeffrey V. Lazarus led the methodology. Jeffrey V. Lazarus, Henry E. Mark, Paul N. Brennan, Christopher J. Kopka, Diana Romero, Dana Ivancovsky Wajcman, and Marcela Villota-Rivas reviewed comments submitted as part of the 2 survey rounds. Jeffrey V. Lazarus, Henry E. Mark, and Marcela Villota-Rivas reviewed all comments sent directly by email. All panel members provided 2 rounds of comments through Qualtrics XM. Henry E. Mark, Marcela Villota-Rivas, and Jeffrey V. Lazarus wrote the first draft of the manuscript, which was reviewed by the core group. Those fulfilling authorship criteria are named.

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CONFLICTS OF INTEREST

Jeffrey V. Lazarus is on the speakers' bureau for AbbVie, Gilead Sciences, Intercept, Janssen, Novo Nordisk, and ViiV. He consults for Novavax. He received grants from AbbVie, Gilead, MSD, and Roche. He has other interests with EASL Public Health and Policy Committee, HIV Outcomes, ISGlobal, the "Generalitat de Catalunya" through the CERCA Program, and SHARE Global Health Foundation. Henry E. Mark consults for the European Association for the Study of The Liver (EASL). Alina M. Allen consults, advises, and received grants from Novo Nordisk. She received grants from Pfizer and Target Pharma. Patrizia Carrieri received grants from Intercept and MSD. Mazen Nouredin consults, advises, and received grants from Echosens, Gilead, GlaxoSmithKline, Madrigal, Novo Nordisk, OWL, Pfizer, Roche, Siemens, Terns, and Takeda. He consults, advises, and owns stock in Cytodyn. He consults and advises 89BIO, Altimmune, Boehringer Ingelheim, Merck, and Prespectum. He received grants from Allergan, Akero, Bristol Myers Squibb, Conatus, Corcept, Enanta, Gilead, Galectin, GENFIT, Novartis, Shire, and Zydus. He received grants and owns stock in Viking. He is employed by Echosens and Incytes and owns stock in Rivus Pharma, CIMA, and ChronWell. William Alazawi consults, advises, is on the speakers' bureau, and received grants from Gilead. He consults, advises, and received grants from, AstraZeneca, GlaxoSmithKline. He advises Novo Nordisk. He is on the speakers' bureau for UCB. He owns stock in Metadeq. Naim Alkhouri consults, is on the speakers' bureau, and received grants from AbbVie/Allergan, Gilead, Intercept, and Perspectum. He consults and is on the speakers' bureau for Echosens. He consults and received grants from Madrigal, Novo Nordisk, Pfizer, and Zydus. He consults for Fibronostics. He is on the speakers' bureau for Alexion, Eisai, Exelixis, Salix, and Theratechnologies. He received grants from 89Bio, Akero, Arbutus, Better Therapeutics, Boehringer

Ingelheim, Bristol Myers Squibb, Corcept, DSM, Galectin, Genentech, Genfit, Hepagene, Healio, Inventiva, Ionis, Merck, NGM, Noom, NorthSea, Poxel, and Viking. Quentin M. Anstee, on behalf of Newcastle University, consults and advises for Alimentiv, Akero, AstraZeneca, Axcella, 89Bio, Boehringer Ingelheim, Bristol Myers Squibb, Galmed, GENFIT, Genentech, Gilead, GlaxoSmithKline, Hanmi, HistolIndex, Intercept, Inventiva, Ionis, IQVIA, Janssen, Madrigal, Medpace, Merck, NGM Bio, Novartis, Novo Nordisk, PathAI, Pfizer, Prosciento, Poxel, Resolution Therapeutics, Ridgeline Therapeutics, Roche, RTI, 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. He serves as coordinator of the IMI2 LITMUS consortium. Ramon Bataller is on the speakers' bureau for AbbVie. Thomas Berg consults, advises, is on the speakers' bureau, received grants, and employed by AbbVie, Gilead, and Intercept. He consults, is on the speakers' bureau, and is employed by Janssen. He consults, is on the speakers' bureau, and received grants from MSD/Merck, Novartis, Orphalan, and Sequana Medical. He consults and is on the speakers' bureau for Alexion, Bayer, Eisai, Ipsen, SIRTEX, and SOBI. He consults and received grants from Humedics. He consults for Enyo Pharma, GlaxoSmithKline, HepaRegeniX GmbH, Roche, and Shionogi. He is on the speakers' bureau for Advance Pharma, Falk Foundation, and MedUpdate GmbH. He received grants from Bristol Myers Squibb, Merz, and Norgine. Paul N. Brennan consults for Resolution Therapeutics. He is on the speakers' bureau for Takeda. Patrizia Burra advises and is on the speakers' bureau for Chiesi Farmaceutici and Gilead. She advises Astellas, Biotest, Kedrion, Novartis, and Sandoz. She is employed by Alpha Wasserman. Helena Cortez-Pinto consults, advises, and is on the speakers' bureau for EISAI and Roche Portugal. She consults for Novo Nordisk and Orphalan. Kenneth Cusi consults and received grants from Novo Nordisk. He consults for Aligos, Allergan, Altimmune, Arrowhead, AstraZeneca, Bristol Myers Squibb, Boehringer Ingelheim, Coherus, Covance, Eli Lilly, Fractyl, Genentech, Gilead, Hanmi, Intercept, Janssen, Madrigal, Pfizer, Prosciento, Sagimet, and Siemens. He received grants from Cirus, Echosens, Inventiva, LabCorp, National Institute of Health, Nordic Bioscience, Novartis, Poxel, and Zydus. Nikos Dedes advises Gilead and GlaxoSmithKline. He has other interests with the Greek Patients Association and the Positive Voice (PLHIV Association). Ajay Duseja has other interests with the Indian National Association for the Study of the Liver (INASL). Sven M. Francque consults, is on the speakers' bureau, and received grants from GENFIT, Gilead, Inventiva, and Merck Sharp & Dome. He consults and is on the speakers' bureau for

AbbVie, Allergan, Bayer, Eisai, Intercept, Novo Nordisk, and Promethera. He consults and received grants from Astellas, Janssen, and Roche. He consults for Actelion, Aelin Therapeutics, Aligos Therapeutics, AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, Coherus, CSL Behring, Echosens, Enyo, Galapagos, Galmed, Genentech, Julius Clinical, Madrigal, Medimmune, NGM Bio, and Novartis. He is on the speakers' bureau for Janssens Cilag. He received grants from Falk Pharma, GlympsBio, Pfizer, and Research Foundation Flanders. Amalia Gastaldelli consults, advises, is on the speakers' bureau, received grants, and employed by Pfizer. She consults, is on the speakers' bureau, received grants, and employed by Eli Lilly. She consults, advises, and is on the speakers' bureau for Boehringer Ingelheim and Novo Nordisk. She consults for Fractyl and Merck Sharp & Dohme. She has other interests with the European NAFLD study group and European Group for Insulin Resistance (EGIR). Hannes Hagström consults and received grants from AstraZeneca. He received grants from EchoSens, Gilead, MSD, and Pfizer. He is employed by MediPlast. Aleksander Krag advises, received grants, and employed by Siemens. He received grants and holds patent rights from the Region of Southern Denmark and the University of Southern Denmark. He advises and is employed by Norgine and Nordic Bioscience. He advises Novo Nordisk. He received grants from AstraZeneca, the Danish National Research Foundation, Echosense, EU Horizon 20, Innovation Fund Denmark, and the Novo Nordisk Foundation. He is employed by Echosens. He holds intellectual property rights with Gyldendal. He has other interests with the European Association for the Study of The Liver (EASL). Philip N. Newsome consults, advises, is on the speakers' bureau, received grants, and is employed by 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. Mary E. Rinella consults for Amgen, CytoDyn, GlaxoSmithKline, HistoIndex, Intercept, Madrigal, NGM Bios, Novo Nordisk, Rivus, and Sonic Incytes. Diana Romero is on the speakers' bureau for the European Association for the Study of The Liver (EASL). Marcelo Silva consults, advises, and received grants from Zydus. He received grants from AstraZeneca, GlaxoSmithKline, Inventiva, Merck, and MSK. He has other interests with ALEH and the Global NASH Council. C. Wendy Spearman is on the speakers' bureau for Abbott. She is on the speakers' bureau and is employed by Gilead. She has other interests with Society on Liver Disease of Africa and the International Advisory Board of The Lancet Gastroenterology and Hepatology Journal. Norah A. Terrault consults for Eiger BioPharmaceuticals, ENYO Pharma, Exigo, and Saol Therapeutics. She is on the speakers' bureau for the Asian Pacific Association for the Study of the Liver (APASL), Canadian Association for the Study of

the Liver (CASL), Duke University, European Association for the Study of the Liver (EASL), Gastroenterology Updates, IBD, Liver Disease (GUILD), Houston Methodist, International Liver Transplantation Society (ILTS), Pakistan Society for the Study of Liver Disease (PSSLD), and University of Alabama, Birmingham (UAB). She received grants from Durect Corp, Genentech-Roche, Gilead, GlaxoSmithKline, Helio Health, and the National Institutes of Health. She has other interests with the American Association for the Study of Liver Diseases (AASLD), Clinical Care Options (CCO), the Hepatitis B Foundation, HBV Forum, Indian National Association for the Study of the Liver (INASL), and Simply Speaking. Emmanuel A. Tsochatzis consults, advises, and is on the speakers' bureau for Novo Nordisk. He consults and advises Boehringer Ingelheim and Pfizer. He is on the speakers' bureau for Dr Falk. He has other interests with EASL Governing Board. Luca Valenti consults, advises, is on the speakers' bureau, and received grants from Gilead. He consults and advises Boehringer Ingelheim, Intercept, Pfizer, Novo Nordisk. He consults for AstraZeneca and Diatech Pharmacogenetics. He is on the speakers' board for AbbVie, Alfa-Sigma, MSD, and Viatrix. He holds intellectual property rights with Takeda. Marcela Villota-Rivas consults for the European Association for the Study of The Liver (EASL). Shira Zelber-Sagi is on the speakers' board for AbbVie. Jörn M. Schattenberg consults, is on the speakers' bureau, and is employed by Gilead. He consults, is on the speakers' bureau, received grants from Boehringer Ingelheim. He consults and is on the speakers' bureau for Madrigal and Novo Nordisk. He consults for Albireo Pharma, Apollo Endosurgery, AstraZeneca, Bayer, Bristol Myers Squibb, GlaxoSmithKline, Intercept, Ipsen, Inventiva, MSD, Northsea Therapeutics, Novartis, Pfizer, Roche, Sanofi, and Siemens Healthineer. He is on the speakers' bureau for Echosens, HistoIndex, and MedPublico GmbH. He received grants from, and Siemens Healthcare GmbH. He owns stock in AGED diagnostics and Hepta Bio. Vincent Wai-Sun Wong consults, is on the speakers' bureau, received grants, and is employed by Gilead. He consults, is on the speakers' bureau, and employed by AbbVie. He consults and is on the speakers' bureau for Novo Nordisk. He consults for Boehringer Ingelheim, Echosens, Intercept, Inventiva, Pfizer, Sagimet, and TARGET PharmaSolutions. He is on the speakers' bureau for Abbott and Unilab. He owns stock in Illuminatio Medical Technology Limited. Zobair M. Younossi consults for Abbott, AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, Cymabay, Gilead, GlaxoSmithKline, Intercept, Madrigal, Merck, Novo Nordisk, Quest, and Siemens. The remaining authors have no conflicts to report.

DATA AVAILABILITY STATEMENT

De-identified source data for all analyses will be made available for fair use by contacting the corresponding

author (Jeffrey.Lazarus@sph.cuny.edu), with appropriate ethical approval.

Authorship list - *Healthy Livers, Healthy Lives*

Collaborators: Jeffrey V. Lazarus^{*1,2,3}, Henry E. Mark^{*4,5}, Alina M. Allen^{*6}, Juan Pablo Arab^{*7,8,9}, Patrizia Carrieri^{*10}, Mazen Nouredin^{*11}, William Alazawi¹², Naim Alkhouri¹³, Saleh A. Alqahtani¹⁴, Quentin M. Anstee¹⁵, Marco Arrese⁹, Ramon Bataller¹⁶, Thomas Berg¹⁷, Paul N. Brennan¹⁸, Patrizia Burra¹⁹, Graciela E. Castro-Narro^{20,21,22}, Helena Cortez-Pinto²³, Kenneth Cusi²⁴, Nikos Dedes²⁵, Ajay Duseja²⁶, Sven M. Francque^{27,28}, Amalia Gastaldelli²⁹, Hannes Hagström³⁰, Terry T-K. Huang^{3,31}, Dana Ivancovsky Wajcman¹, Achim Kautz³², Christopher J. Kopka³³, Aleksander Krag³⁴, Philip N. Newsome³⁵, Mary E. Rinella³⁶, Diana Romero³⁷, Shiv Kumar Sarin³⁸, Marcelo Silva³⁹, C. Wendy Spearman⁴⁰, Norah A. Terrault⁴¹, Emmanuel A. Tsochatzis⁴², Luca Valenti^{43,44}, Marcela Villota-Rivas¹, Shira Zelber-Sagi^{45,46}, Jörn M. Schattenberg^{*47}, Vincent Wai-Sun Wong^{*48}, Zobair M. Younossi^{*49}, Fredrik Aberg⁵⁰, Leon A. Adams⁵¹, Khalid Al-Naamani⁵², Reda M. Albadawy⁵³, Zinaida Alexa⁵⁴, Michael Allison⁵⁵, Faisal Abdullatif Alnaser⁵⁶, Khalid Alswat⁵⁷, Mario R. Alvares-da-Silva⁵⁸, Domenico Alvaro⁵⁹, Michele Alves-Bezerra⁶⁰, Raul J. Andrade⁶¹, Yaw Asante Awuku⁶², Oidov Baatarkhuu⁶³, Gyorgy Baffy⁶⁴, Shokhista R. Bakieva⁶⁵, Meena B. Bansal⁶⁶, Robert Barouki⁶⁷, Rachel L. Batterham⁶⁸, Cynthia Behling⁶⁹, Renata Belfort-DeAguiar⁷⁰, Annalisa Berzigotti⁷¹, Michael Betel⁷², Cristiana Bianco⁷³, Emanuele Bosi⁷⁴, Jerome Boursier⁷⁵, Elizabeth M. Brunt⁷⁶, Elisabetta Bugianesi⁷⁷, Christopher J. Byrne⁷⁸, Maria Cecilia Cabrera Cabrejos⁷⁹, Stephen Caldwell⁸⁰, Rotonya Carr⁸¹, Marlen Ivón Castellanos Fernández⁸², Laurent Castera⁸³, Maria Gabriela Castillo-López⁸⁴, Cyrielle Caussy⁸⁵, Eira Cerda-Reyes⁸⁶, Antonio Ceriello⁸⁷, Wah- Kheong Chan⁸⁸, Yoosoo Chang⁸⁹, Phunchai Charatcharoenwithaya⁹⁰, Norberto Chavez-Tapia⁹¹, Raymond T. Chung⁹², Massimo Colombo⁹³, Kirsten J. Coppel⁹⁴, Helma P. Cotrim⁹⁵, Antonio Craxi⁹⁶, Javier Crespo⁹⁷, Anuradha Dassanayake⁹⁸, Nicholas O. Davidson⁹⁹, Robert J. de Knegt¹⁰⁰, Victor de Ledinghen¹⁰¹, Münevver Demir¹⁰², Hailemichael Desalegn¹⁰³, Moises Diago¹⁰⁴, John F. Dillon⁷⁸, Bruce Dimmig¹⁰⁵, M. Ashworth Dirac¹⁰⁶, Melisa Dirchwolf¹⁰⁷, Jean-François Dufour¹⁰⁸, Karel Dvorak¹⁰⁹, Mattias Ekstedt¹¹⁰, Mohamed El-Kassas¹¹¹, Osama M. Elsanousi¹¹², Ahmed M. Elsharkawy³⁵, Reda M. Elwakil¹¹³, Wayne Eskridge¹¹⁴, Mohammed Eslam¹¹⁵, Gamal Esmat¹¹⁶, Jian- Gao Fan¹¹⁷, Maria Lucia Ferraz¹¹⁸, Robert Flisiak¹¹⁹, Davide Fortin¹⁰, Yasser Fouad¹²⁰, Scott L. Friedman⁶⁶, Michael Fuchs¹²¹, Adrian Gadano¹²², Anja Geerts¹²³, Andreas Geier¹²⁴, Jacob George¹¹⁵, Lynn H. Gerber¹²⁵, Hasmik L. Ghazinyan¹²⁶, Liana Gheorghe¹²⁷, Denise Giangola Kile¹²⁸, Marcos Giralda¹²⁹, George Goh Boon Bee¹³⁰, Nicolas Goossens¹³¹, Isabel Graupera¹³², Henning

Grønbaek¹³³, Saeed Hamid¹³⁴, Vanessa Hebditch¹³⁵, Zachary Henry⁸⁰, Ingrid J. Hickman¹³⁶, L. Ansley Hobbs³, Samantha L. Hocking¹³⁷, Wolf Peter Hofmann¹³⁸, Ramazan Idilman¹³⁹, Paula Iruzubieta⁹⁷, Scott Isaacs¹⁴⁰, Vasily A. Isakov¹⁴¹, Mona H. Ismail¹⁴², Mohammad H. Jamal¹⁴³, Helen Jarvis¹⁴⁴, Peter Jepsen¹³³, François R. Jornayvaz¹⁴⁵, Sudhamshu K.C.¹⁴⁶, Satoru Kakizaki¹⁴⁷, Saul Karpen¹⁴⁸, Takumi Kawaguchi¹⁴⁹, Shelley E. Keating¹⁵⁰, Yousef Khader¹⁵¹, Seung Up Kim¹⁵², Won Kim¹⁵³, David E. Kleiner¹⁵⁴, Ger Koek¹⁵⁵, Narcisse Patrice Joseph Komas¹⁵⁶, Loreta A. Kondili¹⁵⁷, Bart G. Koot¹⁵⁸, Marko Korenjak¹⁵⁹, Eleni Kotsiliti¹⁶⁰, Yiannoula Koulla¹⁶¹, Carina Kugelmas¹⁶², Marcelo Kugelmas¹⁶³, Asma Labidi¹⁶⁴, Naomi F. Lange¹⁶⁵, Mariana Lazo¹⁶⁶, Nathalie Leite¹⁶⁷, Han-Chieh Lin¹⁶⁸, Undram Lkhagvaa⁶³, Michelle T. Long¹⁶⁹, Patricio Lopez-Jaramillo¹⁷⁰, Adelina Lozano¹⁷¹, Maria Paula Macedo¹⁷², Reza Malekzadeh¹⁷³, Giulio Marchesini¹⁷⁴, Sebastian Marciano¹²², Kim Martinez¹⁷⁵, Sophia E. Martínez Vázquez²¹, Lyudmila Mateva¹⁷⁶, José M. Mato¹⁷⁷, Charles N. Mbendi¹⁷⁸, Alexis Gorden McCary¹⁷⁹, Jeff McIntyre¹⁸⁰, Martin McKee¹⁸¹, Juan M. Mendive¹⁸², Ivana Mikolasevic¹⁸³, Pamela S. Miller¹⁸⁴, Tamara Milovanovic¹⁸⁵, Terri Milton¹⁸⁶, Rosalba Moreno-Alcantar¹⁸⁷, Timothy R. Morgan¹⁸⁸, Ayesha A. Motala¹⁸⁹, Jean Muris¹⁹⁰, Carla Musso¹⁹¹, Edna J. Nava-González¹⁹², Francesco Negro¹⁹³, Alexander V. Nersesov¹⁹⁴, Brent A. Neuschwander-Tetri¹⁹⁵, Dafina Nikolova¹⁹⁶, Suzanne Norris¹⁹⁷, Katja Novak¹⁹⁸, Ponsiano Ocama¹⁹⁹, Janus P. Ong²⁰⁰, Arlinking Ong-Go²⁰¹, Charles Onyekwere²⁰², P. Martin Padilla-Machaca²⁰³, Raluca Pais²⁰⁴, Calvin Q. Pan²⁰⁵, Arturo Panduro²⁰⁶, Manas K. Panigrahi²⁰⁷, Georgios Papatheodoridis²⁰⁸, Imran Paruk¹⁸⁹, Keyur Patel²⁰⁹, Carlos Penha-Goncalves²¹⁰, Norma M. Pérez²¹¹, Juanita Pérez-Escobar²¹², Juan M. Pericàs²¹³, Gianluca Perseghin²¹⁴, Mário Guimarães Pessoa²¹⁵, Salvatore Petta²¹⁶, Claudia Pinto Marques Souza de Oliveira²¹⁷, Dorairaj Prabhakaran²¹⁸, Rachel Pryke²¹⁹, Nikolaos Pylsopoulos²²⁰, Atoosa Rabiee²²¹, Alnoor Ramji²²², Vlad Ratziu²²³, Natarajan Ravendhran²²⁴, Katrina Ray²²⁵, Michael Roden²²⁶, Stefano Romeo²²⁷, Manuel Romero-Gómez²²⁸, Yaron Rotman²²⁹, Samir Rouabhia²³⁰, Ian A. Rowe²³¹, Shakhlo Sadirova²³², Maryam Salem Alkhatry²³³, Riina Salupere²³⁴, Sanjaya K. Satapathy²³⁵, Jeffrey B. Schwimmer²³⁶, Giada Sebastiani²³⁷, Lynn Seim²³⁸, Yosuke Seki²³⁹, Abdel Karim Serme²⁴⁰, David Shapiro²⁴¹, Lali Sharvadze²⁴², Jonathan E. Shaw²⁴³, Isaac Thom Shawa²⁴⁴, Thirivikrama Shenoy²⁴⁵, Oren Shibolet²⁴⁶, Yusuke Shimakawa²⁴⁷, Jay H. Shubrook²⁴⁸, Shivaram Prasad Singh²⁴⁹, Edford Sinkala²⁵⁰, Lubomir Skladany²⁵¹, Igor Skrypnik²⁵², Myeong Jun Song²⁵³, Silvia Sookoian²⁵⁴, Joan B Soriano²⁵⁵, Kannan Sridharan²⁵⁶, Norbert Stefan²⁵⁷, Jonathan G. Stine²⁵⁸, Nikos Stratakis¹, Dhastagir Sultan Sheriff²⁵⁹, Shikha S. Sundaram²⁶⁰, Gianluca Svegliati-Baroni²⁶¹, Mark G. Swain²⁶², Frank

Tacke¹⁰², Shahrads Taheri²⁶³, Soek-Siam Tan²⁶⁴, Elliot B. Tapper²⁶⁵, Giovanni Targher²⁶⁶, Eugen Tcaciuc²⁶⁷, Maja Thiele³⁴, Dina Tiniakos²⁶⁸, Ieva Tolmane²⁶⁹, Aldo Torre²⁷⁰, Esther A. Torres²⁷¹, Sombat Treeprasert-suk²⁷², Michael Trenell²⁷³, Svetlana Turcan²⁶⁷, Adela Turcanu²⁶⁷, Jonas Valantinas²⁷⁴, Laurens A. van Kleef¹⁰⁰, Jose Antonio Velarde Ruiz Velasco²⁷⁵, Mette Vesterhus²⁷⁶, Eduardo Vilar-Gomez²⁷⁷, Imam Waked²⁷⁸, Julia Wattacheril²⁷⁹, Heiner Wedemeyer²⁸⁰, Fonda Wilkins²⁸¹, José Willemse²⁸², Robert J. Wong²⁸³, Yusuf Yilmaz²⁸⁴, Hannele Yki-Järvinen²⁸⁵, Ming- Lung Yu²⁸⁶, Volkan Yumuk²⁸⁷, Müjdat Zeybel²⁸⁸, Kenneth I. Zheng²⁸⁹, Ming-Hua Zheng²⁸⁹

1. Barcelona Institute for Global Health (ISGlobal), Hospital Clínic, University of Barcelona, Barcelona, Spain; 2. Faculty of Medicine and Health Sciences, University of Barcelona, Barcelona, Spain; 3. CUNY Graduate School of Public Health and Health Policy (CUNY SPH), New York, NY, USA; 4. European Association for the Study of the Liver (EASL), Geneva, Switzerland; 5. Independent consultant, Nottingham, UK; 6. Division of Gastroenterology and Hepatology, Department of Medicine, Mayo Clinic, Rochester, MN, USA; 7. Division of Gastroenterology, Department of Medicine, Schulich School of Medicine, Western University & London Health Sciences Centre, London, Ontario, Canada; 8. Department of Epidemiology and Biostatistics, Schulich School of Medicine, Western University, London, Ontario, Canada; 9. Department of Gastroenterology, School of Medicine, Pontificia Universidad Católica de Chile, Santiago, Chile; 10. Aix Marseille Univ, Inserm, IRD, SESSTIM, Sciences Economiques & Sociales de la Santé & Traitement de l'Information Médicale, ISSPAM, Marseille, France; 11. Houston Methodist Hospital, Houston Research Institute, Houston, TX, USA; 12. Barts Liver Centre, Blizard Institute, Queen Mary University of London, London, UK; 13. Fatty Liver Program, Arizona Liver Health, Phoenix, AZ, USA; 14. King Faisal Specialist Hospital & Research Centre, Riyadh, Saudi Arabia; 15. Translational & Clinical Research Institute, Faculty of Medical Sciences, Newcastle University, Newcastle upon Tyne, UK; 16. Liver Unit, Hospital Clínic, University of Barcelona, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain; 17. Division of Hepatology, Department of Medicine II, Leipzig University Medical Center, Leipzig, Germany; 18. Division of Hepatology, University of Dundee, Dundee, Scotland, UK; 19. Multivisceral Transplant Unit-Gastroenterology, Department of Surgery, Oncology and Gastroenterology at the Padua University Hospital, Padua, Italy; 20. Department of Hepatology and Transplant, Hospital Médica Sur, Mexico City, Mexico; 21. Department of Gastroenterology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico; 22. Asociación

Latinoamericana para el Estudio del Hígado (ALEH), Santiago, Chile; 23. Clínica Universitaria de Gastroenterología, Laboratório de Nutrição, Faculdade de Medicina, Universidade de Lisboa, Lisbon, Portugal; 24. Division of Endocrinology, Diabetes & Metabolism, Department of Medicine, University of Florida, Gainesville, FL, USA; 25. Greek Patients Association, Athens, Greece; 26. Department of Hepatology, Postgraduate Institute of Medical Education and Research, Chandigarh, India; 27. Department of Gastroenterology and Hepatology, Antwerp University Hospital, Edegem, Belgium; 28. 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; 29. Institute of Clinical Physiology, National Research Council, Pisa, Italy; 30. Department of Medicine, Huddinge, Karolinska Institutet, Stockholm, Sweden; 31. CUNY Center for Systems and Community Design and NYU-CUNY Prevention Research Center, New York, NY, USA; 32. Kautz 5 gUG, Köln, Germany; 33. Independent researcher, Ponte de Lima, Portugal; 34. Department of Gastroenterology and Hepatology, Odense University Hospital, Odense, Denmark; 35. National Institute for Health Research Birmingham Biomedical Research Centre at University Hospitals Birmingham NHS Foundation Trust and the University of Birmingham, Birmingham, UK; 36. Department of Medicine, University of Chicago, Chicago, IL, USA; 37. Department of Community Health and Social Sciences, CUNY Graduate School of Public Health and Health Policy, New York, NY, USA; 38. Department of Hepatology, Institute of Liver and Biliary Sciences, New Delhi, India; 39. Hepatology and Clinical Research Units, Hospital Universitario Austral, Buenos Aires, Argentina; 40. Division of Hepatology, Department of Medicine, Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa; 41. Gastrointestinal and Liver Disease Division, University of Southern California, Los Angeles, CA, USA; 42. UCL Institute for Liver and Digestive Health, Royal Free Hospital, London, UK; 43. Precision Medicine, Biological Resource Center, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; 44. Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy; 45. School of Public Health, Faculty of Social Welfare and Health Sciences, University of Haifa, Haifa, Israel; 46. Department of Gastroenterology, Tel Aviv Medical Centre, Tel Aviv, Israel; 47. Metabolic Liver Research Program, I. Department of Medicine, University Medical Centre Mainz, Mainz, Germany; 48. The Chinese University of Hong Kong, Hong Kong, China; 49. Center for Liver Disease, Inova, Falls Church, VA, USA; 50. Transplantation and Liver Surgery, Helsinki University Hospital, Helsinki, Finland; 51. Medical School, The University of Western Australia, Perth, Western

- Australia, Australia; 52. Department of Internal Medicine, Division of Gastroenterology and Hepatology, Armed Forces Hospital, Muscat, Oman; 53. Gastroenterology, Hepatology & Infectious Diseases Department, Benha University, Benha, Egypt; 54. Republican Clinical Hospital "Timofei Mosneaga", Chişinău, Republic of Moldova; 55. Liver Unit, Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK; 56. Department of Primary Care & Public Health, Faculty of Medicine, Imperial College, London, UK; 57. Liver Disease Research Center, Department of Medicine, College of Medicine, King Saud University, Riyadh, Saudi Arabia; 58. School of Medicine, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil; 59. Department of Translational and Precision Medicine, Sapienza University of Rome, Rome, Italy; 60. Department of Biomedicine, Biotechnology and Public Health, University of Cadiz, Cadiz, Spain; 61. Servicio de Aparato Digestivo, Hospital Universitario Virgen de la Victoria, Instituto de Investigación Biomédica de Málaga y Plataforma en Nanomedicina-IBIMA Plataforma BIONAND, Universidad de Málaga, Málaga, Spain; 62. University of Health and Allied Science, Ho, Ghana; 63. Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia; 64. VA Boston Healthcare System and Harvard Medical School, Boston, MA, USA; 65. Scientific Department, The Research Institute of Virology of the MoH of the Republic of Uzbekistan, Tashkent, Uzbekistan; 66. Icahn School of Medicine at Mount Sinai, New York, NY, USA; 67. Université Paris Cité, Inserm T3S, Paris, France; 68. Centre for Obesity Research, Department of Medicine, University College London, London, UK; 69. Pacific Rim Pathology Group, San Diego, CA, USA; 70. Internal Medicine Department, Yale University, New Haven, CT, USA; 71. Department of Visceral Surgery and Medicine, Bern University Hospital, University of Bern, Bern, Switzerland; 72. Fatty Liver Alliance, Toronto, Ontario, Canada; 73. Precision Medicine Lab, Biological Resource Center, and Transfusion Medicine, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; 74. IRCCS Ospedale San Raffaele, Milan, Italy; 75. Angers University & Angers University Hospital, Angers, France; 76. Dept. of Pathology and Immunology, Washington University School of Medicine, St. Louis, MO, USA; 77. Dept. of Medical Sciences, University of Torino, Torino, Italy; 78. School of Medicine, University of Dundee, Dundee, Scotland, UK; 79. Liver Unit, Hospital G. Almenara, Universidad Mayor de San Marcos, Lima, Peru; 80. Department of Medicine, University of Virginia, Charlottesville, VA, USA; 81. Division of Gastroenterology, Department of Medicine, University of Washington, Seattle, WA, USA; 82. Institute of Gastroenterology, La Havana, Cuba; 83. Université Paris Cité, Department of Hepatology, Hospital Beaujon, AP-HP, Clichy, Paris, France; 84. Departamento Unidad Metabólica, Hospital Universitario Fundación Favaloro, Buenos Aires, Argentina; 85. Endocrinology Diabetes Nutrition Hospices Civils de Lyon, Lyon, France; 86. Central Military Hospital, Asociación Latinoamericana para el Estudio del Hígado, Mexico City, Mexico; 87. IRCCS Multi-Medica, Milan, Italy; 88. Gastroenterology and Hepatology Unit, Department of Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia; 89. Center for Cohort Studies, Total Healthcare Center, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, South Korea; 90. Faculty of Medicine Siriraj Hospital, Bangkok, Thailand; 91. Médica Sur Clinic & Foundation, Mexico City, Mexico; 92. Liver Center, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA; 93. European Association for the Study of the Liver (EASL) International Liver Foundation, Geneva, Switzerland; 94. Department of Medicine, University of Otago, Wellington, New Zealand; 95. School of Medicine, Federal University of Bahia, Salvador, Brazil; 96. School of Medicine, University of Palermo, Palermo, Italy; 97. Gastroenterology and Hepatology Department, Clinical and Translational Research in Digestive Diseases, Valdecilla Research Institute (IDIVAL), Marqués de Valdecilla University Hospital, Santander, Spain; 98. Faculty of Medicine, University of Kelaniya, Kelaniya, Sri Lanka; 99. Washington University School of Medicine, St. Louis, MO 63110, USA; 100. Erasmus MC University Medical Center, Rotterdam, the Netherlands; 101. CHU Bordeaux, Bordeaux, France; 102. Department of Hepatology & Gastroenterology, Charité - Universitätsmedizin Berlin, Berlin, Germany; 103. St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia; 104. Digestive Diseases Department, Hospital General Universitario de Valencia, Valencia, Spain; 105. Banner Liver Support Group, Phoenix, AZ, USA; 106. Department of Family Medicine, University of Washington, Seattle, WA, USA; 107. Liver Unit, Hospital Privado de Rosario, Rosario, Argentina; 108. Centre des Maladies Digestives Lausanne, Lausanne, Switzerland; 109. Fourth Department of Internal Medicine, First Faculty of Medicine, Charles University, Prague, Czech Republic; 110. Department of Health, Medicine and Caring Sciences, Linköping University, Linköping, Sweden; 111. Endemic Medicine Department, Faculty of Medicine, Helwan University, Cairo, Egypt; 112. Department of Surgery, Faculty of Medicine, National Ribat University, Khartoum, Sudan; 113. Tropical Medicine Department, Ain Shams University, Cairo, Egypt; 114. Fatty Liver Foundation, Boise, ID, USA; 115. Storr Liver Centre, Westmead Hospital, Westmead Institute for Medical Research, University of Sydney, Sydney, New South Wales, Australia; 116. Endemic Medicine Department, Cairo University, Cairo, Egypt; 117. Department of Gastroenterology, Xinhua Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai Key Lab of Pediatric

- Gastroenterology and Nutrition, Shanghai, China; 118. Federal University of Sao Paulo, São Paulo, Brazil; 119. Department of Infectious Diseases and Hepatology, Medical University of Bialystok, Bialystok, Poland; 120. Faculty of Medicine, Minia University, Minya, Egypt; 121. Central Virginia VA Health Care System and Virginia Commonwealth University, Richmond, VA, USA; 122. Liver Unit, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina; 123. Department of Gastroenterology & Hepatology, University Hospital Ghent, Ghent, Belgium; 124. Division of Hepatology, University Hospital Wuerzburg, Wuerzburg, Germany; 125. Beatty Liver and Obesity Center, Inova Health System, Falls Church, VA, USA; 126. Nikomed Medical Center, Yerevan, Armenia; 127. Carol Davila University of Medicine and Pharmacy, Bucharest, Romania; 128. Independent participant, Myrtle Beach, SC, USA; 129. Departamento de Gastroenterología, Hospital de Clinicas, Universidad Nacional de Asunción, San Lorenzo, Paraguay; 130. Department of Gastroenterology and Hepatology, Singapore General Hospital, Singapore; 131. Division of Gastroenterology and Hepatology, Geneva University Hospital, Geneva, Switzerland; 132. Liver Unit, Hospital Clínic, FCRB-IDIBAPS, University of Barcelona, Barcelona, Spain; 133. Department of Hepatology and Gastroenterology, Aarhus University Hospital, Aarhus, Denmark; 134. Department of Medicine, Aga Khan University, Karachi, Pakistan; 135. British Liver Trust, Winchester, UK; 136. Department of Nutrition and Dietetics, Princess Alexandra Hospital, Brisbane, Queensland, Australia; 137. Central Clinical School, Faculty of Medicine and Health, University of Sydney, Sydney, New South Wales, Australia; 138. Medical Care Center for Gastroenterology Bayerischer Platz, Berlin, Germany; 139. Department of Gastroenterology, Ankara University School of Medicine, Ankara, Turkey; 140. Department of Medicine, Emory University School of Medicine, Atlanta, GA, USA; 141. Department of Gastroenterology & Hepatology, Federal Research Centre of Nutrition, Biotechnology & Food Safety, Moscow, Russia; 142. King Fahd Hospital of the University, Al-Khobar, and College of Medicine, Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia; 143. Department of Transplantation and Surgery, Kuwait University, Kuwait City, Kuwait; 144. Newcastle University, Newcastle, UK; 145. Geneva University Hospital, Geneva, Switzerland; 146. National Academy of Medical Sciences, Kathmandu, Nepal; 147. Department of Clinical Research, National Hospital Organization Takasaki General Medical Center, Takasaki, Japan; 148. Emory University School of Medicine, Atlanta, GA, USA; 149. Division of Gastroenterology, Department of Medicine, Kurume University School of Medicine, Kurume, Japan; 150. School of Human Movement and Nutrition Sciences, The University of Queensland, Brisbane, Queensland, Australia; 151. Department of Public Health, Jordan University of Science and Technology, Irbid, Jordan; 152. Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea; 153. Department of Internal Medicine, Seoul National University College of Medicine, Seoul Metropolitan Government Boramae Medical Center, Seoul, Republic of Korea; 154. Laboratory of Pathology, Center for Cancer Research, National Cancer Institute, NIH, Bethesda, MD, USA; 155. Maastricht University Medical Center, Maastricht, the Netherlands; 156. Institut Pasteur de Bangui, Bangui, Central African Republic; 157. Center for Global Health, Istituto Superiore Di Sanità (ISS), UniCamillus-Saint Camillus International University of Health Sciences, Rome, Italy; 158. Department of Pediatric Gastroenterology, Emma's Children Hospital, Amsterdam University Medical Center, Amsterdam, the Netherlands; 159. European Liver Patients' Association, Brussels, Belgium; 160. Nature Reviews Gastroenterology & Hepatology, Berlin, Germany; 161. Cyprus Liver Patients Association, Nicosia, Cyprus; 162. Department of Pediatrics, Denver Health Medical Center, Denver, CO, USA; 163. South Denver Gastroenterology, Englewood, CO, USA; 164. Gastroenterology "A" Department, Rabta University Hospital, Faculty of Medicine of Tunis, University of Tunis El Manar, Tunis, Tunisia; 165. Department of Visceral Surgery and Medicine, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland; 166. Urban Health Collaborative, Dornsife School of Public Health, Drexel University, Philadelphia, PA, USA; 167. Department of Internal Medicine, University Hospital Clementino Fraga Filho, School of Medicine, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil; 168. Division of Gastroenterology and Hepatology, Taipei Veterans General Hospital, Taipei, Taiwan; 169. Novo Nordisk A/S, Vandtårnsvej 108-110, 2860 Søborg, Denmark; 170. Masira Research Institute, Medical School, Universidad de Santander (UDES), Bucaramanga, Colombia; 171. Cayetano Heredia Peruvian University, Lima, Peru; 172. iNOVA4Health, NOVA Medical School, Faculdade de Ciências Médicas, NMS, FCM, Universidade NOVA de Lisboa, Lisbon, Portugal; 173. Digestive Disease Research Institute, Tehran University of Medical Sciences, Tehran, Iran; 174. Alma Mater-University of Bologna, Bologna, Italy; 175. GLI, Lakewood, NJ, USA; 176. University Hospital "St Ivan Rilski", Medical University of Sofia, Sofia, Bulgaria; 177. CIC bioGUNE, Technology Park of Bizkaia, Derio, Spain; 178. Service of Hepatology and Gastroenterology, Department of Internal Medicine, University Clinics of Kinshasa, Kinshasa, Democratic Republic of the Congo; 179. Mid-Atlantic Permanente Medical Group, Rockville, MD, USA; 180. Liver Health Programs, Global Liver Institute, Washington, DC, USA; 181. London School of Hygiene & Tropical Medicine, London, UK; 182. La Mina Primary Health Care Academic Centre, Catalan Health Institute, University

- of Barcelona, Barcelona, Spain; 183. Department of Gastroenterology, UHC Rijeka, Rijeka, Croatia; 184. Independent participant, Powell, OH, USA; 185. School of Medicine, University of Belgrade, University Clinical Center of Serbia, Belgrade, Serbia; 186. Independent consultant, Houston, TX, USA; 187. Gastroenterology Department, HE CMN SXXI, IMSS, Mexico City, Mexico; 188. Medical Service, VA Long Beach Healthcare System, Long Beach, CA, USA; 189. University of KwaZulu-Natal, Durban, South Africa; 190. Dept. General Practice, Care and Public Health Research Institute (CAPHRI), Maastricht University, Maastricht, the Netherlands; 191. Diabetes Metabolic Department, Hospital Universitario Fundación Favaloro, Buenos Aires, Argentina; 192. Facultad de Salud Pública y Nutrición, Universidad Autónoma de Nuevo León, Monterrey, Mexico; 193. University of Geneva, Geneva, Switzerland; 194. Department of Gastroenterology, SD Asfendiyarov Kazakh National Medical University, Almaty, Kazakhstan; 195. Saint Louis University, St. Louis, MO, USA; 196. University Clinic for Gastroenterohepatology, University Ss. Cyril and Methodius, Skopje, Macedonia; 197. Department of Hepatology, St James's Hospital, Dublin, Ireland; 198. Dept. of Gastroenterology and Hepatology, University Medical Center Ljubljana, Ljubljana, Slovenia; 199. Makerere University College of Health Sciences, Kampala, Uganda; 200. University of the Philippines Manila, Manila, Philippines; 201. Section of Gastroenterology and Hepatology, University of Santo Tomas Faculty of Medicine and Surgery, Manila, Philippines; 202. Department of Internal Medicine, Lagos State University College of Medicine Ikeja, Lagos, Nigeria; 203. Liver Unit, Guillermo Almenara National Hospital, National University of San Marcos, Lima, Peru; 204. Sorbonne Université, Assistance Publique-Hôpitaux de Paris, Hôpital Pitié-Salpêtrière, Institute of Cardiometabolism and Nutrition, Centre de Recherche Saint Antoine, INSERM UMRS_938 Paris, France; 205. Division of Gastroenterology and Hepatology, NYU Langone Health, NYU Grossman School of Medicine, New York, NY, USA; 206. Genomic Medicine in Hepatology, Hospital Civil de Guadalajara/CUCS, UdeG, Guadalajara, Mexico; 207. All India Institute of Medical Sciences, Bhubaneswar, India; 208. Medical School of National and Kapodistrian University of Athens, Athens, Greece; 209. University Health Network, Toronto, Ontario, Canada; 210. Instituto Gulbenkian de Ciência, Oeiras, Portugal; 211. Gastroenterologia-Hepatologia-Trasplante Hepático, Hospital General de la Plaza de la Salud, Santo Domingo, Dominican Republic; 212. Gastroenterology Department, Hospital Juárez de México, Mexico City, Mexico; 213. Liver Unit, Vall d'Hebron University Hospital, Vall d'Hebron Institute for Research, Centros de Investigación Biomédica en Red Enfermedades Hepáticas y Digestivas (CIBERehd), Barcelona, Spain; 214. Department of Medicine and Surgery, Università degli Studi di Milano-Bicocca, Milan, Italy; 215. Division of Gastroenterology and Hepatology, University of São Paulo School of Medicine, São Paulo, Brazil; 216. Section of Gastroenterology and Hepatology, PROMISE, University of Palermo, Palermo, Italy; 217. Department of Gastroenterology, University of São Paulo School of Medicine, São Paulo, Brazil; 218. Centre for Chronic Disease Control, New Delhi, India; 219. Bewdley Medical Centre, Bewdley, UK; 220. Rutgers New Jersey Medical School, Newark, NJ, USA; 221. Washington DC VA Medical Center, Washington DC, USA; 222. University of British Columbia, Vancouver, British Columbia, Canada; 223. Sorbonne Université, Paris, France; 224. Department of Hepatology, Johns Hopkins School of Medicine, Baltimore, MD, USA; 225. Nature Reviews Gastroenterology & Hepatology, London, UK; 226. Department of Endocrinology and Diabetology, Medical Faculty, Heinrich Heine University, University Hospital, Düsseldorf, Germany; 227. Department of Molecular and Clinical Medicine, Gothenburg University, Cardiology Department, Sahlgrenska University Hospital, Gothenburg, Sweden; 228. Digestive Diseases Department and CIBERehd, Virgen del Rocío University Hospital, Institute of Biomedicine of Seville (HUVR/CSIC/US), University of Seville, Seville, Spain; 229. Liver & Energy Metabolism Section, Liver Diseases Branch, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institutes of Health (NIH), Bethesda, MD, USA; 230. Internal Medicine Department, Touhami Benflis University Hospital Centre, Batna, Algeria; 231. University of Leeds, Leeds, UK; 232. The Research Institute of Virology of the MoH of the Republic of Uzbekistan, Tashkent, Uzbekistan; 233. Ibrahim bin Hamad Obaidullah Hospital, Emirates Health Services, RAK, UAE; 234. Tartu University Hospital, University of Tartu, Tartu, Estonia; 235. North Shore University Hospital, Zucker School of Medicine at Hofstra/Northwell Health, Hempstead, NY, USA; 236. Division of Gastroenterology, Hepatology, and Nutrition, Department of Pediatrics, University of California San Diego School of Medicine, La Jolla, CA, USA; 237. Division of Gastroenterology and Hepatology, Department of Medicine, McGill University Health Centre, Montreal, Quebec, Canada; 238. American Liver Foundation, West Orange, NJ, USA; 239. Weight Loss and Metabolic Surgery Center, Yotsuya Medical Cube, Tokyo, Japan; 240. University Joseph KI-ZERBO, Ouagadougou, Burkina Faso; 241. Integrated Quality Resources, San Diego, CA, USA; 242. Infectious Diseases, AIDS and Clinical Immunology Research Center, Tbilisi, Georgia; 243. Baker Heart and Diabetes Institute, Melbourne, Victoria, Australia; 244. University of Derby, Derby, UK; 245. Sree Gokulam Medical College and Research Foundation, Venjaramoodu, India; 246. Department of Gastroenterology & Hepatology, Tel Aviv Medical Center & Tel Aviv University, Tel Aviv, Israel; 247. Institut Pasteur, Université Paris Cité,

Unité d'Épidémiologie des Maladies Émergentes, Paris, France; 248. Touro University California, Vallejo, CA, USA; 249. Kalinga Gastroenterology Foundation, Cuttack, India; 250. The University of Zambia, School of Medicine, Department of Internal Medicine, Lusaka, Zambia; 251. HEGITO Liver & Transplant Unit, Dept. Internal Medicine 2 of the Slovak Medical University, F.D. Roosevelt Teaching Hospital, Banská Bystrica, Slovakia; 252. Internal Medicine №1 Department, Poltava State Medical University, Poltava, Ukraine; 253. Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea; 254. 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; 255. Respiratory Department, Hospital Universitario de la Princesa, Madrid, Spain; 256. Arabian Gulf University, Manama, Bahrain; 257. University Hospital of Tübingen, Tübingen, Germany; 258. Penn State Health Milton S. Hershey Medical Center, Hershey, PA, USA; 259. Anna Medical College, Montagne Blanche, Mauritius; 260. Digestive Health Institute, Children's Hospital Colorado, University of Colorado School of Medicine, Aurora, CO, USA; 261. Liver Injury and Transplant Unit, Polytechnic University of Marche, Ancona, Italy; 262. Department of Medicine, University of Calgary, Calgary, Alberta, Canada; 263. Hamad Medical Corporation, Doha, Qatar; 264. Department of Hepatology, Selayang Hospital, Batu Caves, Malaysia; 265. University of Michigan, Ann Arbor, MI, USA; 266. Section of Diabetes and Endocrinology, University of Verona, Verona, Italy; 267. Discipline of Gastroenterology, Nicolae Testemitanu State University of Medicine and Pharmacy, Chişinău, Republic of Moldova; 268. Dept. of Pathology, Aretaieion Hospital, Medical School, National and Kapodistrian University of Athens, Athens, Greece; 269. Riga East University Hospital, University of Latvia, Riga, Latvia; 270. Metabolic Unit, Instituto Nacional de Ciencias Médicas y Nutrición "Salvador Zubirán", Mexico City, Mexico; 271. Department of Medicine, University of Puerto Rico School of Medicine, San Juan, Puerto Rico; 272. Chulalongkorn University, Bangkok, Thailand; 273. Faculty of Medical Sciences, Newcastle University, Newcastle upon Tyne, UK; 274. Vilnius University Hospital Santaros Clinics, Vilnius, Lithuania; 275. Hospital Civil de Guadalajara Fray Antonio Alcalde, Guadalajara, Mexico; 276. Dept. of Clinical Science, University of Bergen, Dept. of Medicine, Haraldsplass Deaconess Hospital, Bergen, Norway; 277. Indiana University School of Medicine, Indianapolis, IN, USA; 278. National Liver Institute, Shebeen El-Kom, Egypt; 279. Department of Medicine, Division of Digestive and Liver Diseases, Columbia University Irving Medical Center, Center for Liver Disease and Transplantation,

New York, NY, USA; 280. Department of Gastroenterology, Hepatology, Infectious Diseases and Endocrinology, Hannover Medical School, Hannover, Germany; 281. Lexington Medical Center, West Columbia, SC, USA; 282. Dutch Liver Patients Association, Hoogland, the Netherlands; 283. Division of Gastroenterology and Hepatology, Stanford University School of Medicine, Veterans Affairs Palo Alto Healthcare System, Palo Alto, CA, USA; 284. Department of Gastroenterology, School of Medicine, Recep Tayyip Erdoğan University, Rize, Turkey; 285. University of Helsinki and Minerva Foundation Institute for Medical Research, Helsinki, Finland; 286. Hepatobiliary Division, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, School of Medicine, College of Medicine, National Sun Yat-sen University, Kaohsiung, Taiwan; 287. Istanbul University-Cerrahpaşa, Cerrahpaşa Medical Faculty, Division of Endocrinology, Metabolism and Diabetes, Istanbul, Turkey; 288. Department of Gastroenterology and Hepatology, Koç University, Istanbul, Turkey; 289. MAFLD Research Center, Department of Hepatology, the First Affiliated Hospital of Wenzhou Medical University, Wenzhou, China

ORCID

Jeffrey V. Lazarus  <https://orcid.org/0000-0001-9618-2299>

Henry E. Mark  <https://orcid.org/0000-0002-8022-4279>

Alina M. Allen  <https://orcid.org/0000-0002-8393-8410>

Juan Pablo Arab  <https://orcid.org/0000-0002-8561-396X>

Patrizia Carrieri  <https://orcid.org/0000-0002-6794-4837>

Mazen Nouredin  <https://orcid.org/0000-0003-2127-2040>

William Alazawi  <https://orcid.org/0000-0002-3891-5914>

Naim Alkhouri  <https://orcid.org/0000-0001-9872-2391>

Saleh A. Alqahtani  <https://orcid.org/0000-0003-2017-3526>

Quentin M. Anstee  <https://orcid.org/0000-0002-9518-0088>

Ramon Bataller  <https://orcid.org/0000-0002-1119-7799>

Thomas Berg  <https://orcid.org/0000-0003-0003-6241>

Paul N. Brennan  <https://orcid.org/0000-0001-8368-1478>

Patrizia Burra  <https://orcid.org/0000-0002-8791-191X>

Graciela E. Castro-Narro  <https://orcid.org/0000-0001-7511-5396>

Helena Cortez-Pinto  <https://orcid.org/0000-0002-8537-8744>

Kenneth Cusi  <https://orcid.org/0000-0002-8629-418X>

Ajay Duseja  <https://orcid.org/0000-0003-3590-2664>

Sven M. Francque  <https://orcid.org/0000-0002-7527-4714>

Amalia Gastaldelli  <https://orcid.org/0000-0003-2594-1651>

Hannes Hagström  <https://orcid.org/0000-0002-8474-1759>

Terry T.K. Huang  <https://orcid.org/0000-0001-5544-5187>

Dana Ivancovsky Wajcman  <https://orcid.org/0000-0002-6238-3938>

Christopher J. Kopka  <https://orcid.org/0009-0004-7245-9184>

Aleksander Krag  <https://orcid.org/0000-0002-9598-4932>

Philip N. Newsome  <https://orcid.org/0000-0001-6085-3652>

Diana Romero  <https://orcid.org/0000-0002-4832-9564>

Shiv Kumar Sarin  <https://orcid.org/0000-0002-0544-5610>

C. Wendy Spearman  <https://orcid.org/0000-0003-3199-301X>

Norah A. Terrault  <https://orcid.org/0000-0003-4143-1950>

Emmanuel A. Tsochatzis  <https://orcid.org/0000-0001-5069-2461>

Luca Valenti  <https://orcid.org/0000-0001-8909-0345>

Marcela Villota-Rivas  <https://orcid.org/0000-0002-7332-735X>

Jörn M. Schattenberg  <https://orcid.org/0000-0002-4224-4703>

Vincent Wai-Sun Wong  <https://orcid.org/0000-0003-2215-9410>

Zobair M. Younossi  <https://orcid.org/0000-0001-9313-577X>

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