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

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

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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 qualifies to respond; SA, somewhat agree; SD, somewhat disagree.

Jeffrey V. Lazarus, Henry E. Mark, Alina M. Allen, Juan Pablo Arab, and Patrizia Carrieri share equal senior authorship of this paper.

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 fatty liver disease prevalence 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 multisectoral responses and novel collaboration, from reorienting 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)
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)
> 101	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.
[a]Based on World Bank regions.
[b]n = 3 participants are originally from Central Asia.
[c]n = 3 participants work in Central Asia.
[d]Denominator includes n of no response.
[e]Sum 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 research 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

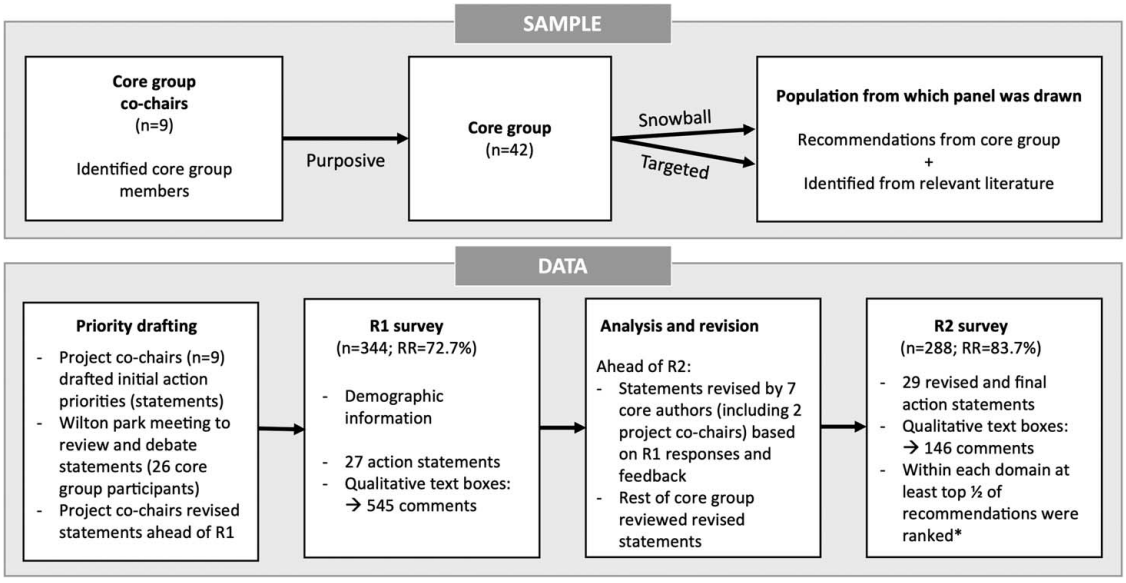

FIGURE 1 Delphi panel generation and data collection.

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

TABLE 2 (*continued*)

Statement		Grade	Rank	A (%)	SA (%)	A + SA (%)	SD (%)	D (%)	NQ (%)	N
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 multimorbidity 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 consensuses 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.

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 Noureddin, 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 and actions. 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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The formation of the Healthy Livers, Healthy Lives global coalition builds on 3 years of work led initially by EILF and since 2021 by EASL. Collaboration has been at the center of this work. Over 500 individuals and organizations spanning over 100 countries have engaged in these efforts, with multiple disciplines and sectors represented, including affected populations. As part of this process, in October 2022, delegates, including representatives from EASL, AASLD, ALEH (representatives from APASL were unable to attend), the Society on Liver Disease in Africa (SOLDA), the European Association for the Study of Diabetes (EASD), the European Association for the Study of Obesity (EASO), the European Society of Primary Care Gastroenterology (ESPCG), the Global NASH Council (GNC), United European Gastroenterology (UEG), the World Obesity Federation (WOF), and the World Organization of Family Doctors (WONCA), gathered for 3 days of discussion at Wilton Park, a UK-based forum for strategic dialogue.

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DATA AVAILABILITY STATEMENT

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

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