Research Article
NAFLD and Alcohol-Related Liver Diseases

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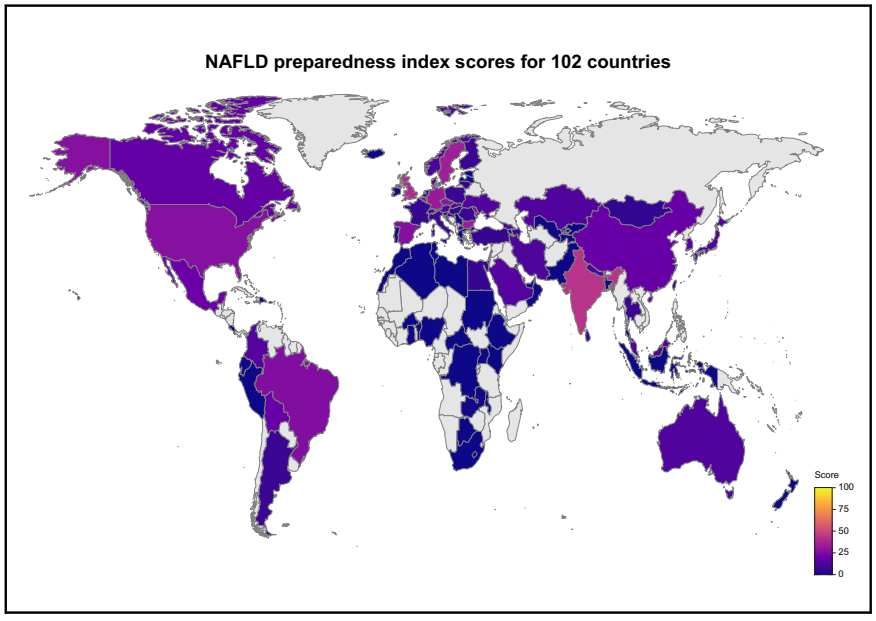
The global NAFLD policy review and preparedness index: Are countries ready to address this silent public health challenge?

Graphical abstract



Highlights

- About a third of countries (n = 32/102) scored zero on the preparedness index.
- No country had a national or sub-national strategy for NAFLD.
- NAFLD was rarely mentioned in the strategies of related conditions such as diabetes.
- Only 32 countries had national NAFLD clinical guidelines.
- A comprehensive NAFLD public health response is lacking in all 102 countries.

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Lay summary

Around a third of the countries scored a zero on the NAFLD policy preparedness index, with no country scoring over 50/100. Although NAFLD is a pressing public health problem, a comprehensive public health response is lacking in all 102 countries. Policies and strategies to address NAFLD at the national and global levels are urgently needed.

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Research Article
NAFLD and Alcohol-Related Liver Diseases

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The global NAFLD policy review and preparedness index: Are countries ready to address this silent public health challenge?

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Background & Aims: Non-alcoholic fatty liver disease (NAFLD) is a highly prevalent, yet largely underappreciated liver condition which is closely associated with obesity and metabolic disease. Despite affecting an estimated 1 in 4 adults globally, NAFLD is largely absent on national and global health agendas.

Methods: We collected data from 102 countries, accounting for 86% of the world population, on NAFLD policies, guidelines, civil society engagement, clinical management, and epidemiologic data. A preparedness index was developed by coding questions into 6 domains (policies, guidelines, civil awareness, epidemiology and data, NAFLD detection, and NAFLD care management) and categorising the responses as high, medium, and low; a multiple correspondence analysis was then applied.

Results: The highest scoring countries were India (42.7) and the United Kingdom (40.0), with 32 countries (31%) scoring zero out of 100. For 5 of the domains a minority of countries were categorised as high-level while the majority were categorised as low-level. No country had a national or sub-national strategy for NAFLD and <2% of the different strategies for related conditions included any mention of NAFLD. National NAFLD clinical guidelines were present in only 32 countries.

Conclusions: Although NAFLD is a pressing public health problem, no country was found to be well prepared to address it. There is a pressing need for strategies to address NAFLD at national and global levels.

Lay summary: Around a third of the countries scored a zero on the NAFLD policy preparedness index, with no country scoring over 50/100. Although NAFLD is a pressing public health problem, a comprehensive public health response is lacking in all 102 countries. Policies and strategies to address NAFLD at the national and global levels are urgently needed.

Keywords: Non-alcoholic fatty liver disease (NAFLD); non-alcoholic steatohepatitis (NASH); liver health; global public health; policy preparedness; health policy; multiple correspondence analysis.
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Introduction

Non-alcoholic fatty liver disease (NAFLD), estimated to affect approximately 25% of the world's adult population,[1,2] is the leading cause of chronic liver disease globally.[3] Around 1 in 5 people with NAFLD develop non-alcoholic steatohepatitis (NASH),[4] which is a leading cause of progression to cirrhosis and hepatocellular carcinoma,[5–7] with liver cancer being the second leading cause of years of life lost amongst all cancers.[8] NAFLD results in sustained healthcare costs and economic losses, and reduced health-related quality of life.[9–14]

NAFLD is considered as the hepatic component of the metabolic syndrome (MetS) and is recognised as part of a multisystem disease.[15–17] NAFLD prevalence is higher in patients with type 2 diabetes mellitus (T2DM) than in the general population, while the incidence of T2DM is higher in patients with NAFLD.[16,18–21] Cardiovascular disease (CVD) is the leading cause of death in patients with NAFLD, followed by extrahepatic malignancies and liver-related complications.[15,16,20,22,23] NAFLD is strongly associated with obesity, with the prevalence increasing proportionally with increases in body mass index,[24] although it can also occur in normal weight individuals, especially in Asian populations.[25,26]

Driven by an increasing prevalence of obesity and T2DM, and an ageing population, the NAFLD burden is projected to grow in the coming decade.[4,27] The clinical management of NAFLD varies depending on the disease stage. Diet and lifestyle changes and the management of underlying metabolic risk factors are the cornerstone of treatment for all patients. In patients at higher risk of disease progression, pharmacologic treatments may be required.[28]

A 2019 study that reviewed the policies and strategies of 29 European countries found that none had a written national strategy specifically for addressing NAFLD and that the disease was mentioned in less than half of all national strategies and clinical management guidelines on cardiovascular disease, obesity, and diabetes.[29] Moreover, international health policy initiatives, including the World Health Organization's (WHO's) universal health coverage programme[30] and the United Nations' Sustainable Development Goals,[31] do not directly include NAFLD or NASH. Awareness of NAFLD amongst the general public, at-risk populations, and non-liver specialist healthcare providers is also low.[32,33]

The first step in designing and delivering a comprehensive public health response to NAFLD is to review the relevant policies and guidelines that are in place. This global NAFLD policy review and preparedness index substantially expands the scope of the earlier European study.[29] In this global study we aim to determine the extent to which governments and key stakeholders are responding to NAFLD and its complications. The findings will help stakeholders, from healthcare providers to policymakers, to identify priority actions that can be taken to better prepare health systems to tackle the current and future burden of this condition.

Materials and methods

Country leads were identified for 168 countries by the European Association for the Study of the Liver (EASL) International Liver Foundation based on their knowledge of relevant national policies and their ability to review documents in the national language(s). Country leads were invited to form a national team to complete 1 survey, working together as a team to reach consensus, prior to submitting the final survey (supplementary material); 129 leads agreed to participate and were sent the survey. Following the invitation, 3 further follow-up emails were sent to leads. A completed survey was received from 73 countries. Experts from 29 European countries that participated in an earlier study in 2019 were invited to update their responses.[29] Initial data collection and updating took place between January and September 2020.

Data validation

Upon submission, survey data from each country were reviewed by a core study team of 3 researchers to ensure accuracy. Source data verification was undertaken and for countries where the relevant documentation (*e.g.* policy, guideline) was available in English, French, or Spanish the core team (JVL, HEM, and MV-R) reviewed these. For documents in other languages, translation software was used and/or country leads were requested to highlight the relevant sections of text in documents. Following the verification process, further clarification was sought from 52 country teams (51% of all countries surveyed). At each validation stage, emphasis was placed on avoiding positive bias in the results (*i.e.* avoiding incorrect positive responses), rather than validating negative responses.

Preparedness index domains

Survey data were used to developed a NAFLD preparedness index, similar to the recently published index for 29 European countries.[34] The main differences between the global and European studies lay in how the categories were defined and the classification of the scores. To estimate the index in this global study, survey questions (n = 20) were grouped into 6 domains and categorised based on criteria determined *a priori* (see Table 1). The criteria for each domain were developed by surveying 9 members of the core author group to reach consensus (Table S1). The policies domain relates to the existence of policies and strategies for NAFLD or the inclusion of NAFLD in policies and strategies for related conditions (*e.g.* T2DM). The guidelines domain relates to the existence of NAFLD clinical guidelines and the inclusion of NAFLD in clinical guidelines for relevant conditions (*e.g.* obesity). The civil awareness domain focuses on the existence of civil society organisations working on NAFLD and national campaigns to raise awareness of the condition. The epidemiology and data domain focuses on the availability of NAFLD data and ongoing efforts to collect such data at the national level. The NAFLD detection domain centres around guidance on screening for NAFLD in specific population groups and the use of algorithms for primary care follow-up. Finally, the NAFLD care management domain relates to guidance on comorbidity screening in patients with NAFLD, which is a necessary step in determining appropriate management approaches, and the involvement of comprehensive care management teams. Each country was classified as low-, middle-, or high-level for each domain based on the criteria in Table 1.

Multiple correspondence analysis

After classifying the countries for each domain, we applied a multiple correspondence analysis (MCA) to calculate a *NAFLD Policy Score* for each country based on their categorised responses and the categorised responses of all other countries in the study. By determining the empirical relationships amongst

Table 1. Criteria for classifying countries in each of the 6 preparedness index domains.

Domain	n*	Low-level (0)	Middle-level (1)	High-level (2)
Policies	4	Did not meet the criteria for high or middle	Had NAFLD mentioned in 2 of the following health strategies**: obesity, diabetes, and liver disease	Had a NAFLD strategy or action plan or had mentioned NAFLD in all strategies covering: obesity, diabetes, and liver disease
Guidelines	4	Did not meet the criteria for high or middle	Had NAFLD mentioned in 2 of the following clinical guidelines: obesity, diabetes, and end-stage liver disease	Had NAFLD guidelines or had NAFLD mentioned in all guidelines on: obesity, diabetes, and end-stage liver disease
Civil awareness	2	Did not meet the criteria for high or middle	Had civil society engagement or a government funded awareness campaign that mentioned NAFLD	Had civil society engagement and a government funded awareness campaign that mentioned NAFLD
Epidemiology and data	3	Did not meet the criteria for high or middle	Had 2 of the following: a population-based epidemiological assessment in the last 5 years, a national or sub-national cohort, or an ongoing epidemiological assessment	Had all of the following: a population-based epidemiological assessment in the last 5 years, a national or regional cohort, and an ongoing epidemiological assessment
NAFLD detection	3	Did not meet the criteria for high or middle	Had 2 of the following: national or sub-national policies/guidelines recommend screening for NAFLD in patients with obesity, national or sub-national policies/guidelines recommend screening for NAFLD in patients with diabetes, or a primary care follow-up algorithm	Had all of the following: national or sub-national policies/guidelines recommend screening for NAFLD in patients with obesity, national or sub-national policies/guidelines recommend screening for NAFLD in patients with diabetes, and a primary care follow-up algorithm
NAFLD care management	4	Did not meet the criteria for high or middle	Had 2 of the following: NAFLD care managed by a multi-disciplinary team, NAFLD guidelines recommend screening for dyslipidaemia, NAFLD guidelines recommend screening for diabetes, or NAFLD guidelines recommend screening for hypertension	Had all of the following: NAFLD care managed by a multi-disciplinary team, NAFLD guidelines recommend screening for dyslipidaemia, NAFLD guidelines recommend screening for diabetes, and NAFLD guidelines recommend screening for hypertension

NAFLD, non-alcoholic fatty liver disease.
*Number of survey questions contributing to each domain.
**A strategy in this context is a wide-ranging document that sets out how to tackle the burden of NAFLD (*i.e.* the broad vision) and includes what the overall goals are, how these will be achieved and the strategic approaches that will be used, and the stakeholders involved.

Table 2. Countries reporting a national or sub-national NAFLD strategy and the inclusion of NAFLD in national or sub-national strategies of related diseases.

Region	n*	NAFLD strategy	Obesity	Alcohol	CVD	Liver disease	Diabetes	Healthy lifestyle /nutrition
East Asia & Pacific	12	0/12 (0%)	0/11 (0%)	0/11 (0%)	0/11 (0%)	0/12 (0%)	0/11 (0%)	0/11 (0%)
Europe & Central Asia	42	0/42 (0%)	2/40 (5%)	1/39 (3%)	1/40 (3%)	1/41 (2%)	0/38 (0%)	1/39 (3%)
Latin America & Caribbean	12	0/12 (0%)	0/12 (0%)	0/12 (0%)	0/12 (0%)	0/12 (0%)	0/12 (0%)	0/12 (0%)
Middle East & North Africa	14	0/14 (0%)	0/13 (0%)	0/14 (0%)	0/13 (0%)	0/14 (0%)	0/13 (0%)	0/14 (0%)
North America	2	0/2 (0%)	0/2 (0%)	0/2 (0%)	0/2 (0%)	0/2 (0%)	0/2 (0%)	0/2 (0%)
South Asia	5	0/5 (0%)	0/5 (0%)	0/5 (0%)	0/5 (0%)	0/5 (0%)	0/5 (0%)	0/4 (0%)
Sub-Saharan Africa	15	0/15 (0%)	0/14 (0%)	0/14 (0%)	0/14 (0%)	0/13 (0%)	0/14 (0%)	0/13 (0%)
Total	102	0/102 (0%)	2/97 (2%)	1/97 (1%)	1/97 (1%)	1/99 (1%)	0/95 (0%)	1/95 (1%)

CVD, cardiovascular disease; NAFLD, non-alcoholic fatty liver disease.
*Denominator for each variable adjusted to remove missing values and responses of "do not know".
East Asia & Pacific: Australia, China, Hong Kong (Special Administrative Region of China), Indonesia, Japan, Republic of Korea, Malaysia, Mongolia, New Zealand, Singapore, Taiwan (China), and Thailand. **Europe & Central Asia**: Armenia, Austria, Azerbaijan, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Georgia, Germany, Greece, Hungary, Iceland, Ireland, Italy, Kazakhstan, Kyrgyz Republic, Latvia, Lithuania, Luxembourg, Moldova (Republic of), Netherlands, North Macedonia, Norway, Poland, Portugal, Romania, Serbia, Slovak Republic, Slovenia, Spain, Sweden, Switzerland, Tajikistan, Turkey, Ukraine, United Kingdom, and Uzbekistan. **Latin America & Caribbean:** Argentina, Aruba, Bahamas, Bolivia, Brazil, Colombia, Costa Rica, Dominican Republic, Ecuador, Mexico, Peru, and Puerto Rico. **Middle East & North Africa**: Algeria, Bahrain, Egypt, Iran (Islamic Republic of), Israel, Kuwait, Lebanon, Libya, Morocco, Oman, Qatar, Saudi Arabia, Tunisia, and United Arab Emirates. **North America:** Canada and United States. **South Asia**: Bangladesh, India, Nepal, Pakistan, and Sri Lanka. **Sub-Saharan Africa:** Benin, Botswana, Burkina Faso, Cabo Verde, Central African Republic, Democratic Republic of the Congo, Ethiopia, Ghana, Kenya, Malawi, Nigeria, South Africa, Sudan, Uganda, and Zambia.

the responses, MCA systematically decomposes the variance in this categorical dataset into new dimensions, called components. Each component explains a percentage of the total variation and the first component maximises that percentage. This allows for all the information in the categorical values for the 6 policy domains for all the countries to be combined into a single factor. This factor functions as a weighted summary of the 6 domains, with the goal of maximising the amount of variation explained by such a summary (Fig. S1).

Three reference scenarios ('worst' – low-level in all categories; 'middle' – medium-level in all categories; and 'best' – high-level in all categories) were included in the analysis to contextualise responses ensuring that the minimum score in all domains equated to the worst possible policy score, and the maximum score in all domains equated to the best possible policy score. Values of country scores were rescaled to range from 0 (worst) to 100 (best) using the standard min-max transformation technique.[35]

Microsoft Excel 2017 version 15.31 was used for initial data management and storage. Data were further managed, cleaned, and analysed using R 4.0.2. Data and code to reproduce these analyses are available at: https://osf.io/cswdq/.

Results

Of the 197 countries invited to complete the survey (168 new leads and 29 leads from the original European study from 2019), responses were received from 102 countries (52%), with a combined population of 6.44 billion (accounting for the 86% of the world population). Of the 95 countries not to respond, the largest proportion were in the Latin American and Caribbean region (33/95; 35%), followed by East Asia and Pacific (21/95; 22%), and sub-Saharan Africa (20/95; 21%). The median number of experts in each country team was 5 (min = 1, max = 9, IQR = 4).

No country had a national or sub-national strategy for NAFLD, while 2% or less of the different strategies for related conditions included any mention of NAFLD (Table 2). National clinical guidelines for NAFLD were present in 32/102 countries (31%). Latin America (6/12) and North America (1/2) had the highest proportion of counties with clinical guidelines, while no country in sub-Saharan Africa (0/15) had a NAFLD guideline. A further 12 countries reported using international clinical guidelines in place of national ones. Of the 59 countries to report having clinical guidelines for obesity, 24 of these (41%) explicitly mentioned NAFLD. Diabetes guidelines were in place in 83 countries with 20 (24%) of these including mention of NAFLD (Table 3). Complete country level data are reported in the supplementary material (Tables S2-9).

Table 4 summarises the classification of 102 countries across the 6 preparedness index domains. For 5 of the domains a minority of countries were categorised as high-level while the majority were categorised as low-level. The exception to this was the guidelines domain, where the minority of countries were categorised as medium-level. For the policies domain, all 102 countries were categorised in the low-level. For NAFLD detection, the 5 countries in the high-level were Belgium, Czech Republic, India, Lebanon, and Moldova. For the epidemiology and data category, Australia, Germany, Iran, and Spain were in the high-level.

The first dimension of the MCA accounted for 52.9% of the variation. Fig. S2 presents the relative importance of all the levels for the different indicators as calculated by the MCA to maximise

Table 3. National or sub-national clinical guideline for NAFLD and related diseases and their inclusion of NAFLD.

	NAFLD	ESLD/cirrhosis		LT		Alcohol		Obesity		Dyslipidaemia		Hypertension		IHD		T2DM	
Region (n*)	Guideline, n (%)	Guideline, n (%)	#NAFLD, n (%)	Guideline, n (%)	#NAFLD, n (%)	Guideline, n (%)	#NAFLD, n (%)	Guideline, n (%)	#NAFLD, n (%)	Guideline, n (%)	#NAFLD, n (%)	Guideline, n (%)	#NAFLD, n (%)	Guideline, n (%)	#NAFLD, n (%)	Guideline, n (%)	#NAFLD, n (%)
East Asia & Pacific (12)	3/12 (25)	7/12 (58)	4/7 (57)	7/12 (58)	4/7 (57)	6/12 (50)	1/5~(20)	9/12 (75)	5/9 (56)	11/12 (92)	1/11 (9)	12/12 (100)	1/12 (8)	9/10~(90)	1/9 (11)	12/12 (100)	9/12 (75)
Europe & Central Asia (42)	19/42 (25)	18/42 (43)	7/18 (39)	18/42 (43)	7/18 (39)	28/37~(76)	3/23~(13)	27/39~(69)	11/27 (41)	27/42 (64)	3/26~(12)	33/40~(83)	0/31~(0)	29/40~(73)	1/27~(4)	38/40~(95)	3/37~(8)
Latin America & Caribbean (12)	6/12 (50)	4/12 (33)	0/3~(0)	4/12 (33)	0/3~(0)	6/11~(55)	0/5~(0)	7/12 (58)	3/7 (43)	8/12 (67)	3/8 (38)	11/12 (92)	0/11 (0)	8/12 (67)	0/8 (0)	11/12 (92)	2/11 (18)
Middle East & North Africa (14)	1/14 (7)	3/14 (21)	0/3 (0)	3/14 (21)	0/3 (0)	0/14 (0)	0/0 (0)	6/13~(46)	2/6 (33)	4/13~(31)	0/3~(0)	7/13~(54)	0/7 (0)	5/12~(42)	0/5 (0)	7/13~(54)	3/7 (43)
North America (2)	1/2 (50)	0/1~(0)	0/0~(0)	0/1~(0)	0/0~(0)	2/2 (100)	0/2 (0)	2/2 (100)	1/2 (50)	2/2 (100)	1/2 (50)	2/2 (100)	1/2 (50)	2/2 (100)	1/2 (50)	2/2 (100)	1/2 (50)
South Asia (5)	2/5 (40)	1/5 (20)	0/1 (0)	1/5 (20)	0/1 (0)	1/5 (20)	0/1 (0)	4/5 (80)	2/4 (50)	1/5 (20)	1/1 (100)	5/5 (100)	0/5 (0)	5/5 (100)	0/4~(0)	5/5 (100)	1/5 (20)
Sub-Saharan Africa (15)	0/15 (0)	1/15 (7)	0/1 (0)	1/15 (7)	0/1 (0)	5/13~(38)	0/5 (0)	4/14~(29)	0/4 (0)	4/14~(29)	1/4 (25)	10/14~(71)	0/9~(0)	6/14~(43)	0/5~(0)	10/14~(71)	1/9~(11)
Total (102)	32/102 (31)	34/101~(34)	11/33~(33)	34/101~(34)	11/33~(33)	48/94~(51)	4/41~(10)	59/97~(61)	24/59 (41)	57/100~(57)	10/55~(18)	80/98~(82)	2/77~(3)	64/95~(67)	3/60~(5)	85/98~(87)	20/83~(24)

ESLD, end-stage liver disease; IHD, ischemic heart disease; LT, liver transplantation; NAFLD, non-alcoholic fatty liver disease; T2DM, type 2 diabetes mellitus.

#NAFLD mentioned in guidelines.

~Denominator for each variable adjusted to remove missing values and responses of "do not know".

*__East Asia & Pacific__: Australia, China, Hong Kong (Special Administrative Region of China), Indonesia, Japan, Republic of Korea, Malaysia, Mongolia, New Zealand, Singapore, Taiwan (China), and Thailand. __Europe & Central Asia__: Armenia, Austria, Azerbaijan, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Georgia, Germany, Greece, Hungary, Iceland, Ireland, Italy, Kazakhstan, Kyrgyz Republic, Latvia, Lithuania, Luxembourg, Moldova (Republic of), Netherlands, North Macedonia, Norway, Poland, Portugal, Romania, Serbia, Slovak Republic, Slovenia, Spain, Sweden, Switzerland, Tajikistan, Turkey, Ukraine, United Kingdom, and Uzbekistan. __Latin America & Caribbean:__ Argentina, Aruba, Bahamas, Bolivia, Brazil, Colombia, Costa Rica, Dominican Republic, Ecuador, Mexico, Peru, and Puerto Rico. __Middle East & North Africa__: Algeria, Bahrain, Egypt, Iran (Islamic Republic of), Israel, Kuwait, Lebanon, Libya, Morocco, Oman, Qatar, Saudi Arabia, Tunisia, and United Arab Emirates. __North America:__ Canada and United States. __South Asia__: Bangladesh, India, Nepal, Pakistan, and Sri Lanka. __Sub-Saharan Africa:__ Benin, Botswana, Burkina Faso, Cabo Verde, Central African Republic, Democratic Republic of the Congo, Ethiopia, Ghana, Kenya, Malawi, Nigeria, South Africa, Sudan, Uganda, and Zambia.

the variation explained in the data. The high-level for NAFLD detection and policies contributed the highest positive value to the score whereas the low category for guidelines contributed the largest negative value.

The highest scoring country was India (42.7), followed by the United Kingdom (40.0), Sweden (34.1), Bulgaria (32.9), Germany (32.1), and Belgium (28.7). 32 countries had a score of zero and only 2 countries – India and the United Kingdom – had a better score than the middle reference scenario (Fig. 1; Fig. S1). Both India and the United Kingdom achieved a high score in the guidelines and care management domains, while India also achieved a high score in the NAFLD detection domain. Overall, 41 countries achieved a high score in at least 1 domain, with India being the only country to do so in more than 2 domains. The domain categorisation and overall policy score for all 102 countries is presented in Table S10.

Discussion

This study collected data on the presence of NAFLD relevant policies in 102 countries and calculated a global policy index based on these responses. We assessed countries across 6 key domains that are critical to delivering appropriate responses to tackle the burden of NAFLD. Overall, these findings indicate the urgent need for substantial policy improvement in all 102 countries surveyed in order to control NAFLD in the forthcoming years.

A country's overall policy score provides an indication of their national preparedness to address NAFLD while the country ranking provides insights into how each country performs compared with the others surveyed. India was found to have the highest score, although this fell well below the best-case reference scenario, highlighting the importance of counties prioritising improvements in their overall score, rather than their ranking. The ranking can be of use in helping to identify countries that are performing better and therefore may have useful insights and experiences to share with others.

Of greater importance than the score itself, we provide insight into which domains each country should prioritise in order to improve the level of preparedness to prevent and manage the burden of NAFLD. It is striking that no country reported a written national or sub-national strategy or action plan for addressing NAFLD. We believe that this is both a cause and a consequence of NAFLD being largely absent in the global public health agenda and the absence of approved pharmacological treatments for the disease. This lack of strategic guidance has stifled action at the global, regional, and local levels, which is only just beginning to be addressed.[36] Equally, a lack of awareness of NAFLD and its health and economic impact has resulted in a sense of inertia. The development of global strategic guidance by liver associations and global institutions such as the WHO would help to drive national level action, as has been shown for viral hepatitis.[37,38] The World Health Assembly resolution 67.6 on viral hepatitis, passed in May 2014, recommended that strategies, action plans, and guidelines for hepatitis C virus treatment be developed in each country;[39] a similar resolution for NAFLD is now required. Recognising that NAFLD is closely related to other prevalent non-communicable diseases (NCDs) and the substantial overlap in the strategic approaches needed to address these conditions, means that NAFLD should also be incorporated into key NCD strategies and action plans at the global and national level, something that has been lacking to date.[40,41]

Between 1990 and 2017 deaths and disability-adjusted life years attributable to cirrhosis increased, as did the proportion of all global deaths due to cirrhosis.[7] With the expansion of prevention and treatment measures for viral hepatitis, the impact of NASH is expected to overtake that of hepatitis B and C in the near future.[7] Innovative approaches to prevention and care for chronic liver disease will be needed.[42] While the imperative for action is greatest in countries with an existing high burden of NAFLD, from a preparedness perspective, all countries should take action to alleviate the anticipated future impact of the disease.[4,12,27] This is especially true in locations where the prevalence of obesity and T2DM are high or rapidly increasingly.

Health system responses will vary depending on the local context. It is important to recognise that many national health systems are made up of complex, decentralised structures each with their own unique arrangements related to finance, governance, and policy. Within countries, especially large populous ones, the burden of disease and health needs of the population will also vary, often greatly, between regions/states. We recognise that our survey may have missed pockets of good practice within countries. Conversely, some countries may have scored well vis-à-vis others, yet have regions or states that are less prepared than the country reported as a whole. However, our intention is to provide an overview of national preparedness, which can help to inform discussions and further research at global, national, and local levels. We would stress that in the absence of global and national strategies and guidance, we are unlikely to achieve large-scale, sustained impact in the fight against NAFLD.

In addition to the dearth of strategic guidance, our findings highlight that over two-thirds of countries still lack specific clinical guidelines for NAFLD, with the condition mentioned in very few clinical guidelines for other closely related conditions. One of the most notably findings is that NAFLD is mentioned in fewer than 1 in 4 diabetes guidelines. While collaboration across medical disciplines is challenging, working with others will be essential to ensure that NAFLD is adequately captured in all relevant clinical guidelines as a means of achieving timely

Table 4. Categorisation of scores across the 6 policy domains for all countries (n = 102).

Policy domain	Low-level, n (%)	Medium-level, n (%)	High-level, n (%)
Policies	102 (100%)	0 (0%)	0 (0%)
Guidelines	65 (64%)	5 (5%)	32 (31%)
Civil awareness	62 (61%)	31 (30%)	9 (9%)
Epidemiology and data	91(89%)	7 (7%)	4 (4%)
NAFLD detection	77 (75%)	20 (20%)	5 (5%)
NAFLD care management	75 (73%)	23 (23%)	4 (4%)

NAFLD, non-alcoholic fatty liver disease.

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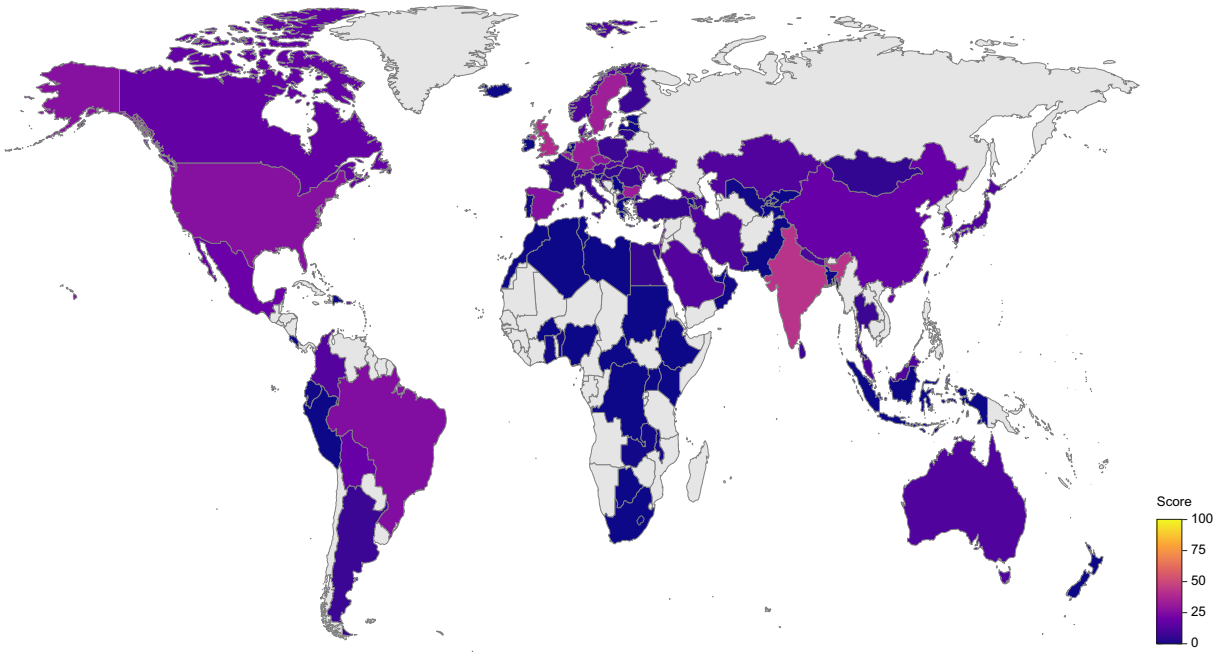

Fig. 1. NAFLD preparedness index scores for 102 countries. This figure shows the *NAFLD Policy Score* for participating countries (n = 102); the score was created using multiple correspondence analysis. NAFLD, non-alcoholic fatty liver disease.

diagnosis, linkage to care, and appropriate multi-disciplinary care for affected individuals.[43] National and regional disease associations play a critical role in providing such guidance. EASL, the European Association for the Study of Diabetes (EASD), and the European Association for the Study of Obesity (EASO) have joint guidance for the management of NAFLD. The American Association for the Study of Liver Diseases (AASLD),[44] the Latin American Association for the Study of the Liver (ALEH),[45] and the Asian Pacific Association for the Study of the Liver (APASL)[46] have all published guidelines. Notably, no country in sub-Saharan Africa had a national NAFLD clinical guideline. In the absence of national guidance, those from international organisations can be used to fill the void, as was the case in 12 countries participating in this study. The WHO package of essential NCD interventions for primary healthcare in low resources settings, while not mentioning NAFLD directly, includes guidance on diabetes management and health promotion, and can therefore be used as a basis for integrating NAFLD care into related disease areas.[47]

In our study, the NAFLD detection domain included screening for NAFLD in people living with obesity and/or T2DM. We appreciate that this is not recommended by all national or international guidance. EASL, EASD, and EASO recommend screening for NAFLD in people with obesity, MetS, and in particular T2DM,[48] and similar recommendations have been made by ALEH[45] and APASL.[46] The American Diabetes Association recommends screening for NASH and advanced fibrosis in patients with elevated liver function tests or hepatic steatosis on ultrasound.[49] In contrast, AASLD does not recommend systematic screening in these groups given the lack of data on cost-effectiveness.[44]

In a recent publication, European NAFLD policy index scores were presented for 29 countries.[34] Data from these 29 countries were updated as necessary and then included in the current analysis. There are several methodological differences between the current analysis and the European analysis, which resulted in changes in the score of all 29 countries. In the current study, 6 domains were used to calculate the policy score, compared to 4 in the European study. The number of domains was increased in order to provide greater granularity in the results and allow for more specific inferences to be made about the actions each country should prioritise to improve their overall policy score. The criteria for classifying countries within each domain were also amended based on global expert opinion. Lastly, the addition of other countries helped to calibrate the scores.

This study has several limitations. The cross-sectional design cannot account for how a country's policy score may have changed over time. This is a general issue in policy evaluation as this is a dynamic field with temporal changes. We plan to overcome this by conducting this survey every 2-4 years. A major challenge with this study is that the data reflect the existence of policies, not the effectiveness of their implementation. Future studies that leverage additional sources of information and engage different stakeholder groups, including patient organisations, will be needed to understand the policy implementation gap. Our data do however provide a baseline for such research and highlight key areas that should be addressed within each country. We recognise that reducing the burden of NAFLD will require action across a range of disciplines and sectors. We address this in part by including information from other disciplines, especially related diseases such as T2DM and obesity, in the score. We do, however, acknowledge that the score does not take into account policies aimed at addressing important cross-cutting issues, such as social inequalities; such considerations will be important for future research.

The survey was self-administered with small national teams working together to provide information. The data used in the index rely on accurate reporting by the country teams. Detailed

instructions were provided to all country teams and when a country team requested clarification about the survey instrument the response was provided to all country teams. To minimise the risk of misreporting we implemented a number of validation checks. Upon submission, all surveys were reviewed by a central research team with responses being cross-checked against available documentation to ensure accuracy and validity. Where necessary, clarification or further information were requested from the country teams. Despite these measures, we cannot fully exclude the possibility that country teams interpreted certain questions differently or that responses were not accurately reported. The low overall scores across counties would, however, indicate a lack of overall positive bias within the results.

Finally, the stability of scores derived from the MCA rely on the pattern in the data and need to be calibrated to provide a direction to the data. We have sought to address this by including 3 reference countries, which helps to contextualise the estimates.

Conclusions

Despite being a highly prevalent liver disease that can lead to severe health, economic, and social consequences, in this global study of 102 countries NAFLD was found to be receiving far too little attention in national health agendas, with around a third of countries scoring a zero on the preparedness index. Countries must make substantial improvements in all 6 domains reported in this study including the strategic, policy, and clinical management levels in order to adequately address this public health challenge; leadership from international organisations such as the WHO will be critical to support national efforts.

Abbreviations

AASLD, American Association for the Study of Liver Diseases; ALEH, Latin American Association for the Study of the Liver; APASL, Asian Pacific Association for the Study of the Liver; CVD, cardiovascular disease; EASD, European Association for the Study of Diabetes; EASL, European Association for the Study of the Liver; EASO, European Association for the Study of Obesity; MCA, multiple correspondence analysis; MetS, metabolic syndrome; NAFLD, non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis; NCD, non-communicable disease; T2DM, type 2 diabetes mellitus; WHO, World Health Organization.

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Conflict of interest

HEM, MV-R, and AP report receiving consulting fees from the EASL International Liver Foundation related to this work. The EASL International Liver Foundation received grants from Intercept, Bristol-Myers-Squibb Company, Genfit, and MSD to support this study. The funders played no role in the conceptualisation, design, data collection, analysis, decision to publish, or preparation of the manuscript. All other authors declare no relevant completing interests.

Please refer to the accompanying ICMJE disclosure forms for further details.

Authors' contributions

JVL conceived of the article, developed the preliminary outline, and led the development of the questionnaire with QMA and HCP. JVL, HEM, and MV-R led the data collection. AP led the development of the methods and analysis related to the estimation of the index. MV-R, HEM, and JVL verified the data. JVL and HM wrote the first draft with input from MV-R, AP, QMA, and HCP. All authors contributed to and reviewed the full draft of the article, subsequent revisions, and approved the final version for submission.

Data availability statement

Data and code to reproduce the analyses of this manuscript are available on OSF, with identifier NAFLD global index at: https://osf.io/cswdq/.

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Supplementary data

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